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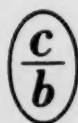
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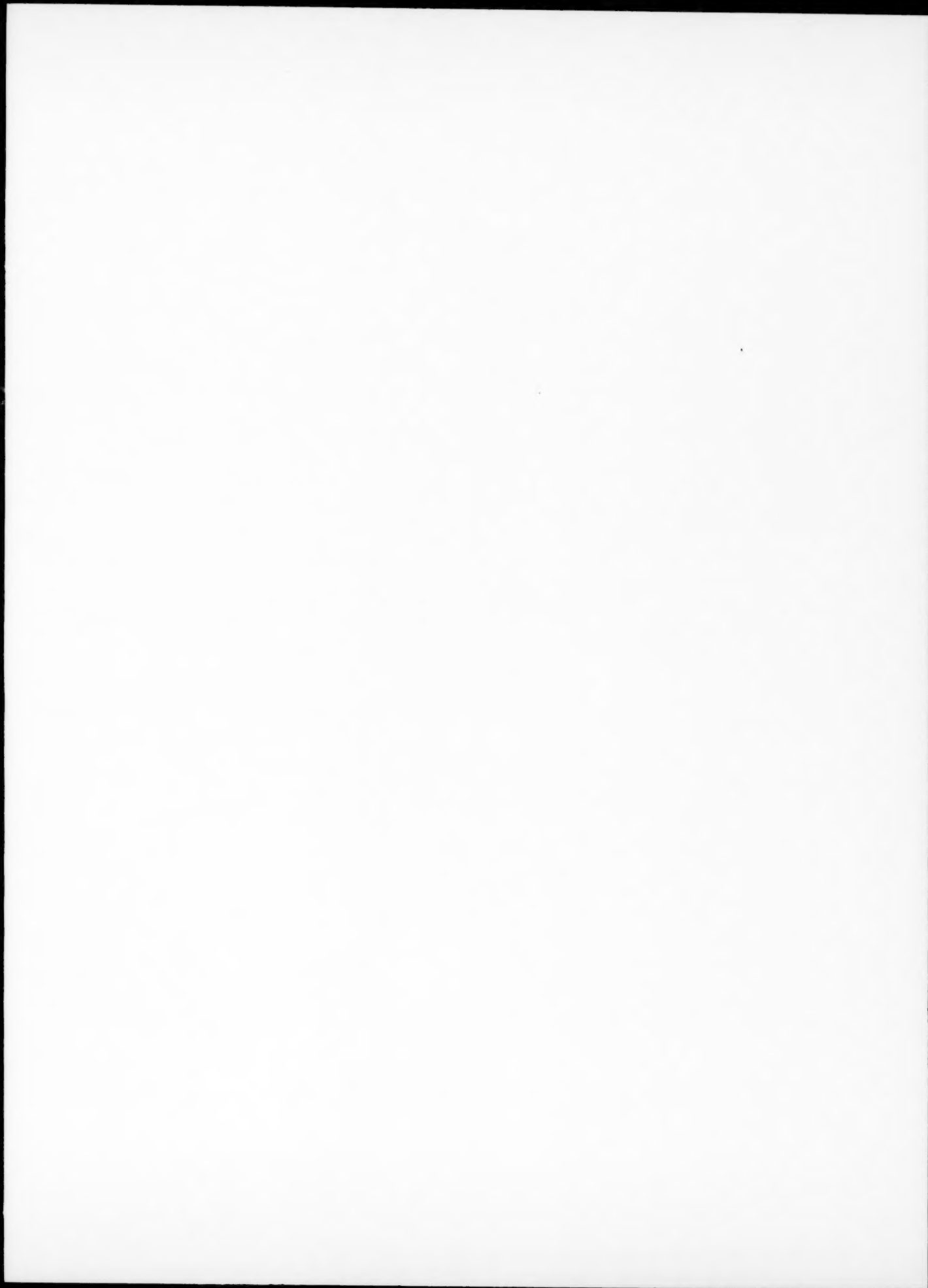
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(ZHURNAL OBSHCHEI KHIMII)

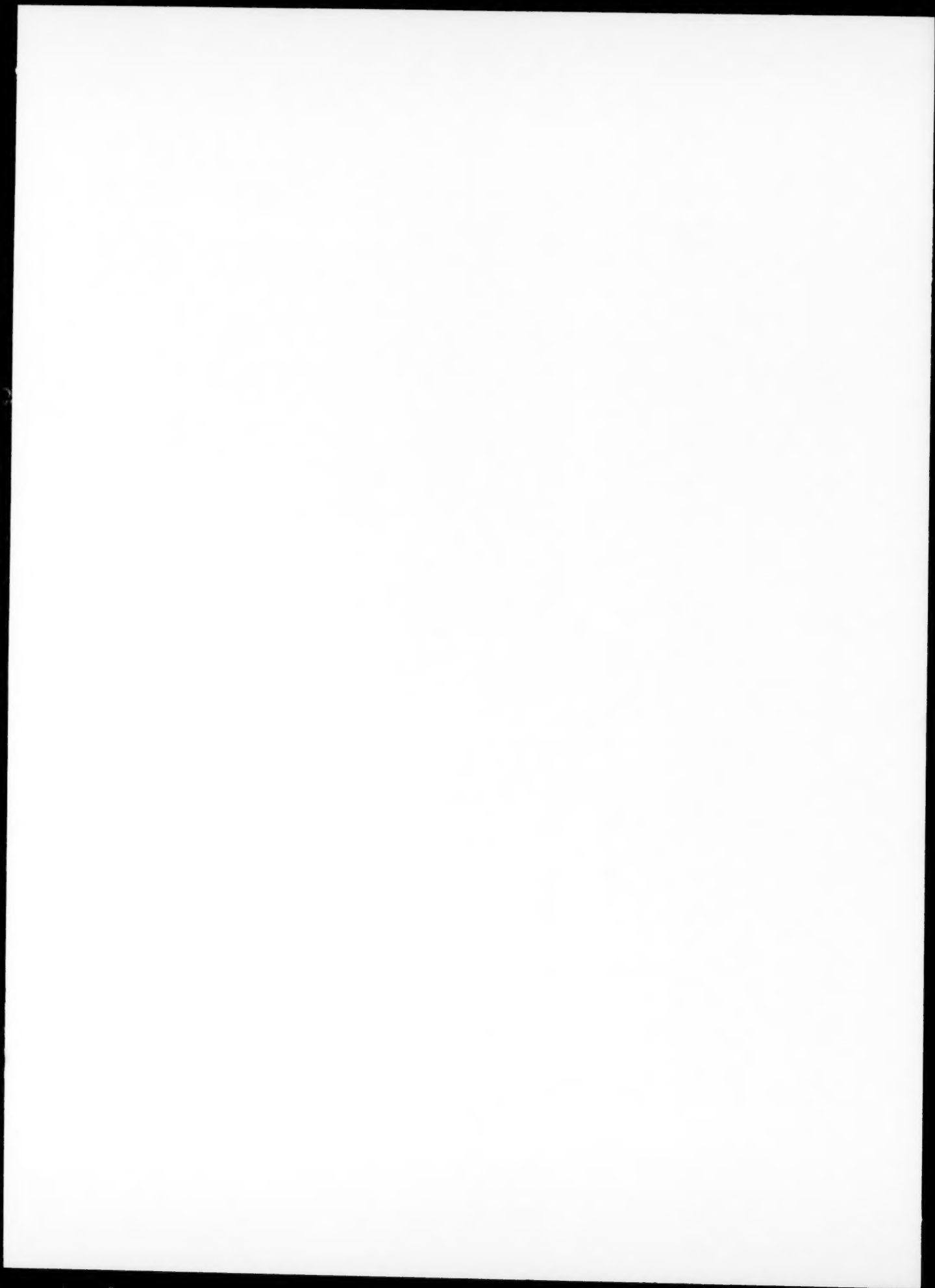
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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LEIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.- Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.



The Editorial board of Zhurnal Obshchei Khimii congratulates Corresponding Member of the Academy, Professor Nikolai Ignat'evich Nikitin, on the occasion of his seventieth birthday, and wishes him many years of good health and success in his work.

ADIAGONAL RECIPROCAL TERNARY SYSTEM OF SODIUM AND POTASSIUM BUTYRATES AND ACETATES

N. M. Sokolov and É. I. Pochtakova

Smolensk Medical Institute

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Investigation of a reciprocal ternary system, on three sides of which complex formation occurs, is of definite interest. The data obtained may be compared with the results of investigations conducted earlier [1,2].

The properties of the initial components of the system — sodium and potassium acetates and butyrates — were set forth by us in detail earlier [1,2]. In the present work, recrystallized C.P. commercial acetates were used. The butyrates were synthesized, proceeding from butyric acid, and the corresponding bicarbonates according to directions given earlier [3]. The dry salts were then recrystallized from butanol. The melting points of the salts are: sodium acetate 331°, potassium acetate 301°, sodium butyrate 330°, and potassium butyrate 404°. The following polymorphic conversions were established for them earlier: CH_3COONa at 254° [4], CH_3COOK at 58 and 155°, $\text{C}_3\text{H}_7\text{COONa}$ at 117, 232, 252, and 316°, and $\text{C}_3\text{H}_7\text{COOK}$ at 190, 285, and 345° [5].

EXPERIMENTAL

The work was done by the visual-polythermal method of physicochemical analysis, using the customary procedure. The results of the investigation are given in the tables and shown in the figures. All percentages are molar.

Binary Systems

1. System $\text{CH}_3\text{COONa}-\text{CH}_3\text{COOK}$. Earlier [1], we mentioned complex formation here for the first time. Now the system has been restudied. The three branches of the melting-point curve intersect at the eutectic points 235° and 53.5% CH_3COOK , and 240° and 61.5% CH_3COOK .

2. System $\text{C}_3\text{H}_7\text{COONa}-\text{C}_3\text{H}_7\text{COOK}$. We described this earlier [2]. Here a continuous series of solid solutions without any extremum occurs.

3. System $\text{CH}_3\text{COONa}-\text{C}_3\text{H}_7\text{COONa}$. This was described earlier as a system with complex formation [3]. The three branches of the melting-point curve intersect at two eutectic points, at 266° and 33.5% $\text{C}_3\text{H}_7\text{COONa}$, and 250° and 69% $\text{C}_3\text{H}_7\text{COONa}$. Presumably the composition of the compound is $3\text{CH}_3\text{COONa} \cdot 2\text{C}_3\text{H}_7\text{COONa}$.

4. System $\text{C}_3\text{H}_7\text{COOK}-\text{CH}_3\text{COOK}$. This is described for the first time (Table 1). The three branches of the melting-point curve intersect at the transition point 350° and 20.5% and the eutectic point 273° and 85.5% CH_3COOK . Presumably the composition of the compound is $6\text{C}_3\text{H}_7\text{COOK} \cdot \text{CH}_3\text{COOK}$.

Diagonal Sections

1. $\text{CH}_3\text{COONa}-\text{C}_3\text{H}_7\text{COOK}$ passes through the field of the component CH_3COONa , the field of the compound $3\text{CH}_3\text{COONa} \cdot 2\text{C}_3\text{H}_7\text{COONa}$, and the field of solid solutions. The three branches of crystallization intersect at 220° and 29% $\text{C}_3\text{H}_7\text{COOK}$ and at 200° and 44.5% $\text{C}_3\text{H}_7\text{COOK}$ (Table 1).

TABLE 1

Binary system $C_3H_7COOK-CH_3COOK$		Diagonal sections			
		$CH_3COONa-C_3H_7COOK$		$CH_3COOK-C_3H_7COONa$	
mole % CH_3COOK	temp.	mole % C_3H_7COOK	temp.	mole % C_3H_7COONa	temp.
0	404°	0	331°	0	301°
10	386	5	312	5	285
15	377	10	296	10	268
20	355	15	273	15	249
20.5	350	20	252	15.5	246
22.5	347	25	236	20	244
25	344	30	219	25	243
30	338	35	214	35	237
40	326	40	203	40	229
45	321	42.5	201	45	221
50	319	44.5	200	48	217
60	311	45	202	50	210
77.5	288	50	234	55	249
82.5	278	55	261	65	281
85.5	273	65	309	75	312
87.5	278	75	341	85	326
90	284	85	372	90	328
100	301	90	384	95	329
		95	391	100	330
		100	404		

TABLE 2

Point	Character of point	Temperature	Composition (mole %)		
			CH_3COONa	CH_3COOK	C_3H_7COONa
E	Eutectic	180°	26	45	20
P ₁	Transition	199	9	47.5	43.5
P ₂	The same	185	27	51	22
R	Peritectic	191	29	55	16

2. $CH_3COOK-C_3H_7COONa$ passes through the field of the component CH_3COOK , the field of the compound $6C_3H_7COOK \cdot CH_3COOK$, and the field of solid solutions. The three branches of crystallization intersect at 246° and 15.5% C_3H_7COONa and at 217° and 48% C_3H_7COONa (Table 1).

Internal Sections

In order to bring out the crystallization fields and to find the triple nonvariant points, 22 internal sections were studied, the trend of which is shown in Fig. 3, and the melting-point curves, in Figs. 1 and 2.

A projection of the crystallization surface of the three-dimensional diagram on the composition square (Fig. 3) was constructed from the results of investigation of binary systems and diagonal and internal sections. The liquidus surface of the system consists of six fields. The field of solid solutions is retained within the system and occupies 43.7%, the field of the compound $6C_3H_7COOK \cdot CH_3COOK$ occupies 21.6%, the field of CH_3COONa 16%, the field of the compound $3CH_3COONa \cdot 2C_3H_7COONa$, 11.9%, the field of CH_3COOK , 5.6%, and the field of the compound $2CH_3COONa \cdot 3CH_3COOK$, 1.2% of the total liquidus-surface area of the system. The lines of cocrystallization of the fields intersect at the eutectic point E, two transition points P_1 and P_2 , and one peritectic point R. The temperature and composition of each point are given in Table 2.

Adiagonal system. The entire liquidus surface of the system is divided by three lines, originating at the hypothetical poles of the compounds $3CH_3COONa \cdot 2C_3H_7COONa$ and $6C_3H_7COOK \cdot CH_3COOK$, into four phase triangles:

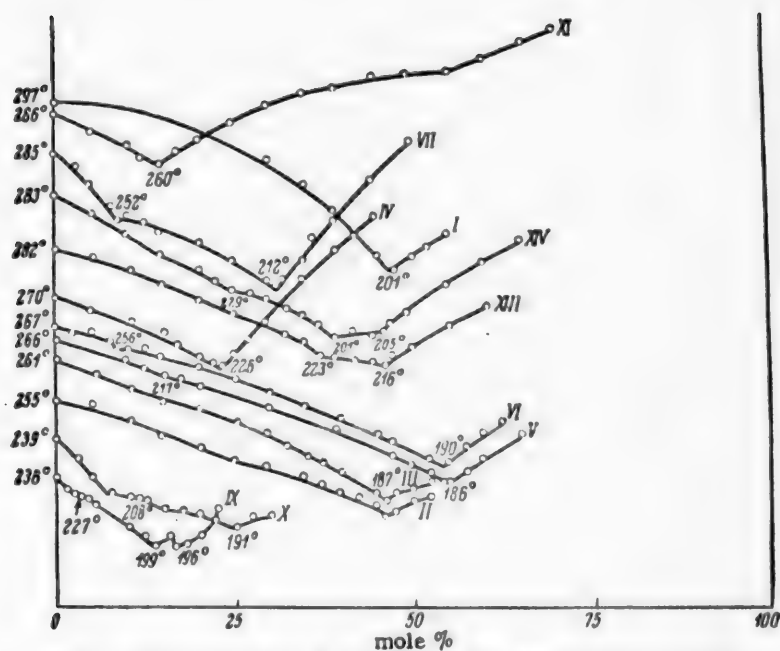


Fig. 1. Internal sections of the system Na, K||CH₃COO, C₃H₇COO.

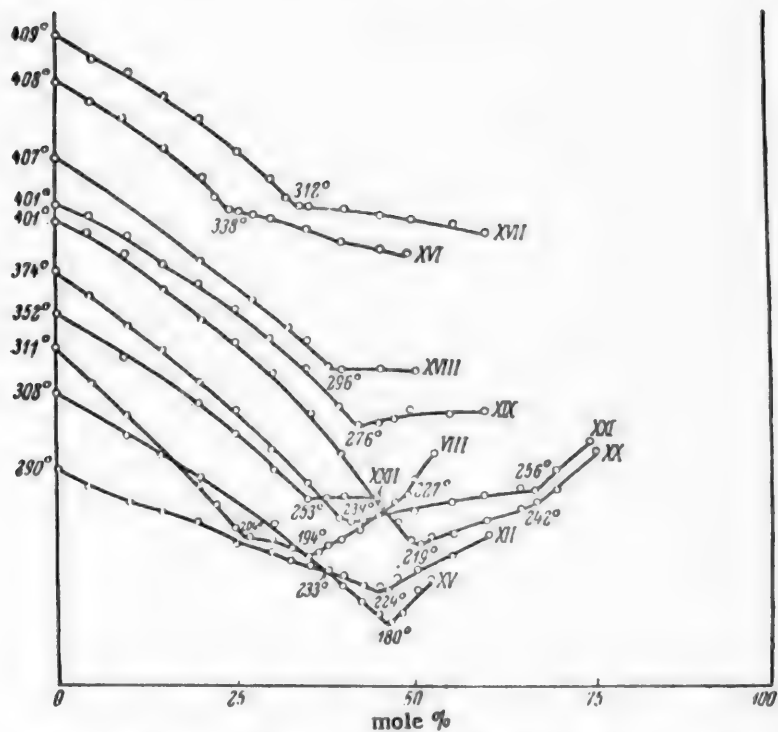


Fig. 2. Internal sections of the system Na, K||CH₃COO, C₃H₇COO.

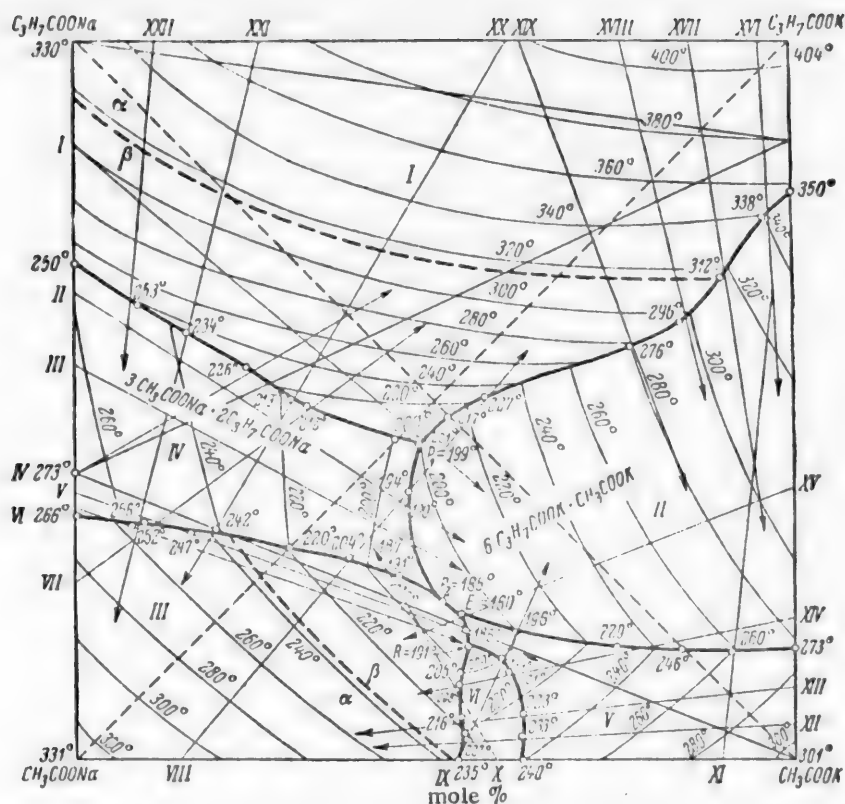


Fig. 3. Projection of the three-dimensional diagram of the system Na, K||CH₃COO, iso-C₃H₇COO on the composition square.

- 1) C₃H₇COONa-C₃H₇COOK-6C₃H₇COOK · CH₃COOK,
- 2) 6C₃H₇COOK · CH₃COOK-C₃H₇COONa-3CH₃COONa · 2C₃H₇COONa with transition point P₁,
- 3) 3CH₃COONa · 2C₃H₇COONa-6C₃H₇COOK · CH₃COOK-CH₃COOK with eutectic point E,
- 4) CH₃COOK-3CH₃COONa · 2C₃H₇COONa-CH₃COONa with transition point P₁ and peritectic point R.

DISCUSSION OF RESULTS

The presence of anionic complexes on opposite sides of the system square suppressed the exchange reaction; complex formation predominates in the system. The system is of the adiaxonal-zonal type. On comparing the present system with the diagonal system of sodium and potassium acetates and propionates [1], we see that replacement of propionates by butyrates sharply changed the character of the system. In the propionate system the presence of cationic complexes on opposite sides of the system square had no effect on the exchange reaction—both compounds tapered off and ended at peritectic points. However, the presence of anionic complexes in the system of sodium and potassium thiocyanates and butyrates [2] also had no effect on the exchange reaction. In the present system, as in the propionate system, the compound 3CH₃COOK · 2CH₃COONa tapers off, but in the present system it occupies a somewhat greater portion of the liquidus surface. Unfortunately, owing to the absence of literature data on the heats of formation of propionates, butyrates, and their compounds, we cannot relate all the facts obtained to the energetics of exchange and complex-formation processes, but are restricted to the mere statement of them.

SUMMARY

1. The liquidus surface of the reciprocal ternary system of sodium and potassium butyrates and acetates was studied for the first time.

* As in original — Publisher's note.

2. Data on the binary system of potassium acetate and butyrate are given for the first time.
 3. The formation of a compound in the system of sodium and potassium acetates was again confirmed.
- In conclusion, we consider it our pleasant duty to thank A. G. Bergman for valuable advice.

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RECIPROCAL TERNARY SYSTEM OF SODIUM AND POTASSIUM ISOBUTYRATES AND ACETATES

N. M. Sokolov and É. I. Pochtakova

Smolensk Medical Institute

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Earlier it was shown that in heteroanionic binary systems of the sodium salts of fatty acids, branching of the carbon chain in the fatty-acid salt radical quite definitely affects processes in the melts; however, no such effect is observed in systems of fatty-acid potassium salts [1-4]. Hence, it is of interest to investigate systems whose components are the sodium and potassium salts of iso-acids.

Commercial C.P. preparations of sodium and potassium acetates, recrystallized beforehand, were used for the work. The isobutyrate were prepared from commercial "pure" grade isobutyric acid, distilled beforehand, and C. P. sodium and potassium bicarbonates by a method described earlier [1]; the dry salts were then recrystallized from butanol. The solidification (melting) points of the salts were: CH_3COONa , 331°; CH_3COOK , 301°; iso- $\text{C}_3\text{H}_7\text{COONa}$, 262°; and iso- $\text{C}_3\text{H}_7\text{COOK}$, 360°. Polymorphic conversions were established earlier [5] for these salts by the method of differential-thermal analysis, as follows: CH_3COONa at 254° [6], CH_3COOK at 58 and 155°, iso- $\text{C}_3\text{H}_7\text{COONa}$ at 67, 91, and 220°, and iso- $\text{C}_3\text{H}_7\text{COOK}$ at 208, 273, and 348°. The salts melt without decomposition.

EXPERIMENTAL

The work was done by the visual-polythermal method of physicochemical analysis, using the customary procedure. The results of the investigation are given in the tables and shown in the figures. The composition of the mixtures is expressed everywhere in mole percent.

*Original Russian pagination. See C. B. translation.

TABLE 1

Binary systems				Diagonal sections			
iso- $\text{C}_3\text{H}_7\text{COONa}$ -iso- $\text{C}_3\text{H}_7\text{COOK}$		iso- $\text{C}_3\text{H}_7\text{COOK}$ - CH_3COOK		CH_3COONa -iso- $\text{C}_3\text{H}_7\text{COOK}$		CH_3COOK -iso- $\text{C}_3\text{H}_7\text{COONa}$	
mole % iso- $\text{C}_3\text{H}_7\text{COOK}$	temp.	mole % CH_3COOK	temp.	mole % iso- $\text{C}_3\text{H}_7\text{COOK}$	temp.	mole % iso- $\text{C}_3\text{H}_7\text{COONa}$	temp.
0	262°	0	360°	0	331°	0	301°
5	254	5	352	10	296	5	290
7.5	248	10	343	20	262	7.5	285
10	255	20	320	30	226	10	279
15	266	25	310	35	200	11	276
20	277	27.5	304	36.5	191	12.5	275
25	285	30	298	37.5	192	17.5	267
30	293	32	294	40	195	25	255
35	302	32.5	296	45	200	35	229
40	308	35	297	47.5	202	45	206
45	315	40	301	48	202	47.5	197
50	320	50	304	50	209	49	193
55	325	55	304	52.5	224	50	205
60	331	60	305	55	232	60	218
65	335	70	302	60	251	65	224
70	338	75	298	65	268	75	225
75	342	85	294	70	281	80	225
80	345	86.5	291	75	296	85	224
85	348	87.5	293	80	309	86	223
90	353	90	294	85	323	87.5	228
95	357	95	298	95	344	90	238
100	360	100	301	100	360	100	262

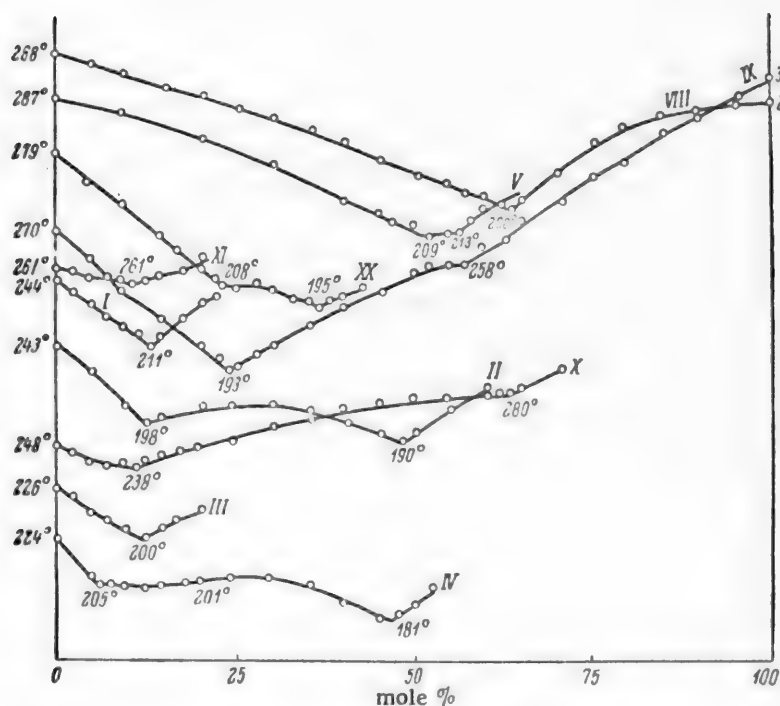
Fig.1 . Internal sections of the reciprocal ternary system $\text{Na, K}||\text{CH}_3\text{COO, iso-C}_3\text{H}_7\text{COO}$.

TABLE 2

No. of phase triangle	Vertices of the phase triangle	Character and temperature of the nonvariant point	Comp. corresponding to the nonvariant point			
			CH ₃ COONa	CH ₃ COOK	iso-C ₃ H ₇ COONa	iso-C ₃ H ₇ COOK
I	CH ₃ COOK · 2 iso-C ₃ H ₇ COONa—iso-C ₃ H ₇ COONa—iso-C ₃ H ₇ COOK	P 209°	7.5	15.5	—	77
II	CH ₃ COOK · 2 iso-C ₃ H ₇ COONa—iso-C ₃ H ₇ COOK—3CH ₃ COOK · 2 iso-C ₃ H ₇ COOK	P 192	4.5	49.5	46	—
III	CH ₃ COOK · 2 iso-C ₃ H ₇ COONa—CH ₃ COONa—iso-C ₃ H ₇ COONa	E 196	23	13	64	—
IV	CH ₃ COOK · 2 iso-C ₃ H ₇ COONa—CH ₃ COONa—3CH ₃ COOK · 2 iso-C ₃ H ₇ COOK	E 182	18	48.5	33.5	—
V	3CH ₃ COOK · 2 iso-C ₃ H ₇ COOK—3CH ₃ COOK · 2CH ₃ COONa—CH ₃ COONa	E 194	29.5	52.5	18	—
VI	3CH ₃ COOK · 2 iso-C ₃ H ₇ COOK—2CH ₃ COONa · 3CH ₃ COOK—CH ₃ COOK	P 205	30	56	14	—

Binary Systems

1. CH₃COONa—CH₃COOK. Complex formation in this system was mentioned earlier [7]. The three branches of the melting-point curve intersect in eutectic points at 235° and 53.5% CH₃COOK, and at 240° and 61.5% CH₃COOK.

2. CH₃COONa—iso-C₃H₇COONa. This was described earlier [1]. The two branches of the melting-point curve intersect in a eutectic point at 208° and 58% iso-C₃H₇COONa.

3. iso-C₃H₇COONa—iso-C₃H₇COOK. The two branches of the melting-point curve intersect in a eutectic point at 248° and 7.5% iso-C₃H₇COOK [8] (Table 1).

4. iso-C₃H₇COOK—CH₃COOK. This was investigated by us for the first time. The three branches of the melting curve intersect in two eutectic points: at 294° and 32% CH₃COOK, and at 291° and 86.5% CH₃COOK. Presumably, the composition of the compound is 3CH₃COOK · 2iso-C₃H₇COOK (Table 1).

Diagonal Sections

1. CH₃COONa—iso-C₃H₇COOK. This passes through the CH₃COONa field, the field of the compound CH₃COOK · 2iso-C₃H₇COONa, and the iso-C₃H₇COOK field. The three branches of the melting-point curve intersect at 191° and 36.5% iso-C₃H₇COOK, and at 202° and 48% iso-C₃H₇COOK (Table 1).

2. CH₃COOK—iso-C₃H₇COONa. This passes through the field of the compound 3CH₃COOK · 2iso-C₃H₇COOK, the iso-C₃H₇COOK field, and the iso-C₃H₇COONa field. The four branches of the melting-point curve intersect in three points: at 276° and 11% iso-C₃H₇COONa, 193° and 49% iso-C₃H₇COONa, and 225° and 86% iso-C₃H₇COONa (Table 1).

Internal Sections of the System

In order to delimit the crystallization fields of the liquidus surface of the system, it was necessary to investigate 20 internal sections, whose trend is shown in Fig. 3. The melting-point curves of the sections are shown in Figs. 1 and 2.

The liquidus diagram of the reciprocal system was constructed on the basis of two diagonals and twenty internal sections (Fig. 3). The liquidus surface of the system consists of seven crystallization fields: Four fields correspond to the four corners of the composition square, two correspond to compounds formed on the sides of the system square, and one to a heteroionic compound. The largest portion of the square—33.6%—is occupied by the iso-C₃H₇COOK field, 24.4% by the field of the compound 3CH₃COOK · 2iso-C₃H₇COOK, 23.8% by the

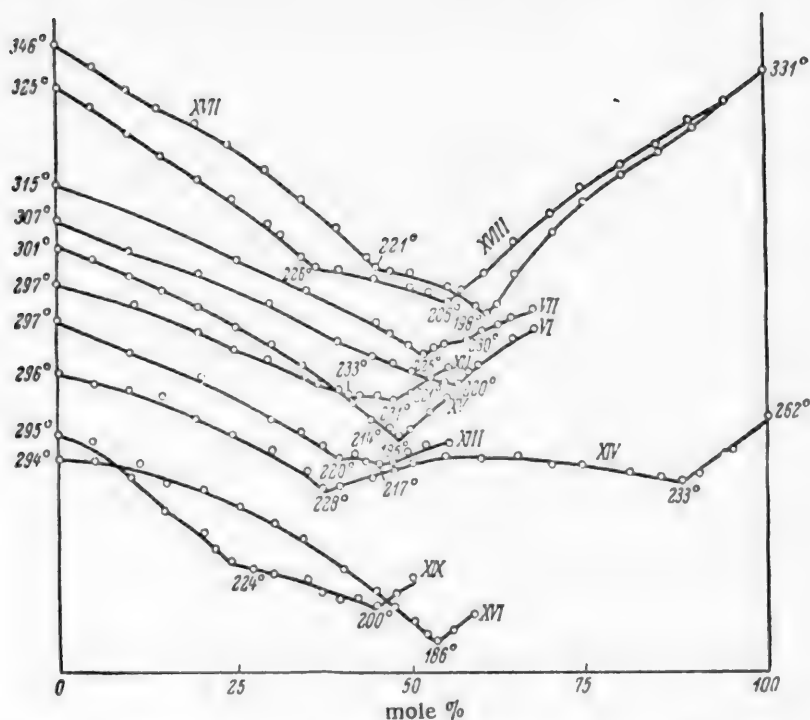


Fig. 2. Internal sections of the reciprocal ternary system Na, K||CH₃COO, iso-C₃H₇COO.

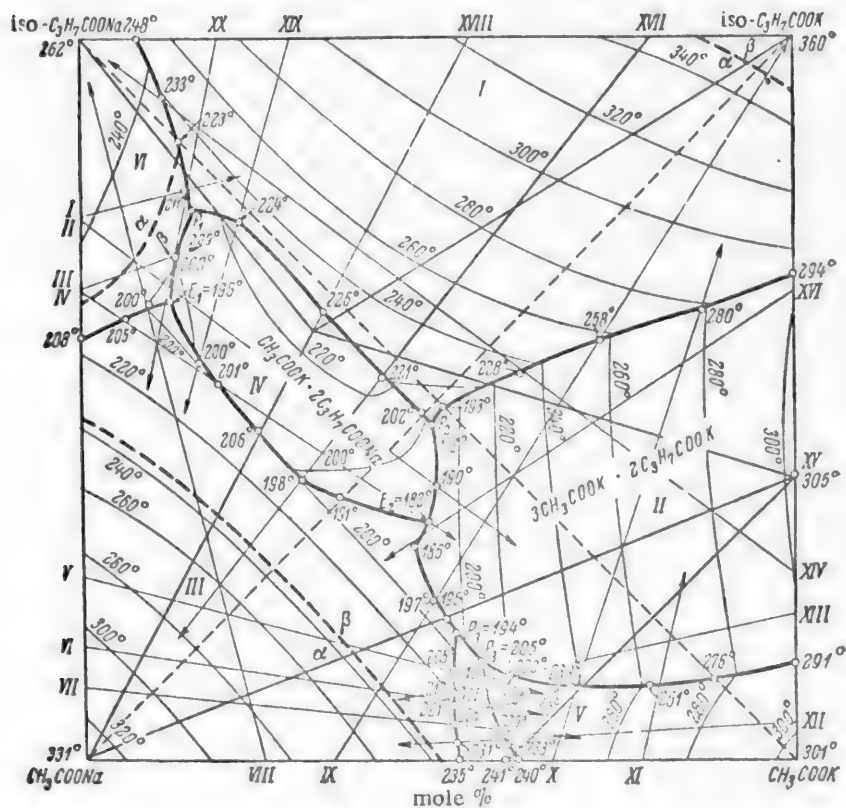


Fig. 3. Projection of the three-dimensional diagram of the reciprocal ternary system Na, K||CH₃COO, iso-C₃H₇COO on the composition square.

CH₃COONa field, 7.8% by the field of the heteroionic compound CH₃COOK · 2 iso-C₃H₇COONa; 4.9% by the CH₃COOK field, 4.6% by the iso-C₃H₇COONa field, and 0.9% by the field of the compound 3CH₃COOK · 2CH₃COONa.

Six triangulating sections, of which four originate at the pole of the heteroionic compound and two at the pole of the compound formed on the lateral side of the system square, divide the entire reciprocal system into six phase triangles with a triple nonvariant point in each.

All data on the phase triangles are given in Table 2.

DISCUSSION OF RESULTS

In this system, complex-formation processes predominate; the system is adlagonal. Within the system, probably owing to the interaction of iso-C₃H₇COONa with the compound 3CH₃COOK · 2 iso-C₃H₇COOK, a heteroionic compound with the probable formula 2 iso-C₃H₇COONa · CH₃COOK is formed. In the field of the heteroionic compound this formula corresponds to the composition having the highest melting point, 226° (33% CH₃COOK, 60% iso-C₃H₇COONa, and 7% CH₃COONa). On triangulation we took this composition for the pole of the compound; however, it must be noted that the field of the compound is somewhat inclined to the diagonal, possibly displaced by the highest-melting component — iso-C₃H₇COOK.

On comparing the configuration of the field of the compound formed on the lateral side of the square in the present system, namely 2CH₃COONa · 3CH₃COOK, with that in systems where the second components were salts with a straight chain of carbon atoms in the radical (Na, K || C₂H₅COO, CH₃COO [7], and Na, K || C₃H₇COO, CH₃COO [8]), in the case of which it tapers off and ends in peritectic points, it is evident that replacement of the salt by the isobutyrate stabilized this compound. In all these systems, this compound occupies, on the average, about 1% of the liquidus surface of the system.

SUMMARY

1. The liquidus surface of the reciprocal ternary system of sodium and potassium acetates and isobutyrate was investigated for the first time.

2. Data on the binary systems iso-C₃H₇COONa—iso-C₃H₇COOK and iso-C₃H₇COOK—CH₃COOK are reported for the first time.

In conclusion, we thank A. G. Bergman for valuable advice.

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*Original Russian pagination. See C. B. translation.

EQUILIBRIA IN THE SYSTEMS

SATURATED HETEROPOLYACIDS - ORGANIC SOLVENTS

E. A. Nikitina and E. V. Prytkova

All-Union Scientific Research Institute of Chemical Reagents

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Systems of the most important heteropolyacids and water have often been the object of investigation [1]; the solubility of heteropolyacids in organic solvents has hardly been studied. In the present article, the results of a systematic investigation of the solubility of the heteropolyacids phosphotungstic, phosphomolybdic, silicotungstic, and silicomolybdic acids in alcohols (ethyl, propyl, and especially isoamyl), as well as certain data on the solubility of heteropolyacids in ethyl ether and acetone, are set forth.

Initial Compounds and Analytical Procedure

We prepared phosphomolybdic acid by a nonether method [2], phosphotungstic acid by a method using ether [3], and silicomolybdic [4] and silicotungstic acids by a nonether method. The resulting higher hydrates of heteropolyacids were dehydrated in desiccators, first over H_2SO_4 , and then over P_2O_5 . After 20 days of drying over phosphoric anhydride the following heteropolyacid hydrates were obtained: $H_7[P(Mo_2O_7)_6] \cdot 5.5H_2O$, $H_7[P(W_2O_7)_6] \cdot 2.5H_2O$, $H_8[Si(Mo_2O_7)_6] \cdot 7H_2O$, and $H_8[Si(W_2O_7)_6] \cdot 5H_2O$. These hydrates, containing relatively small quantities of water of hydration, were recrystallized from ethyl and propyl alcohols, dried in air, and analyzed. Recrystallization from the alcohols led to the formation of mixed solvates of heteropolyacids, containing water and an alcohol (hydratoalcoholates). Thus, recrystallization from ethyl alcohol gave compounds of the compositions: $H_7[P(W_2O_7)_6] \cdot 1.5H_2O \cdot 2C_2H_5OH$, $H_7[P(Mo_2O_7)_6] \cdot 4.5H_2O \cdot C_2H_5OH$, $H_8[Si(Mo_2O_7)_6] \cdot 5H_2O \cdot C_2H_5OH$, and $H_8[Si(W_2O_7)_6] \cdot 3H_2O \cdot 2C_2H_5OH$. Recrystallization from propyl alcohol gave hydratoalcoholates of the compositions: $H_7[P(W_2O_7)_6] \cdot 1.5H_2O \cdot 2.5C_3H_7OH$ and $H_7[P(Mo_2O_7)_6] \cdot 3.5H_2O \cdot 1.5C_3H_7OH$. Phosphomolybdic acid crystallized slowly from alcohols, a viscous, dark green solution being formed. Recrystallization was carried out in desiccators or in the air.

The ethyl and propyl alcohols which we used in the investigation were dehydrated over potassium carbonate and calcium oxide and distilled. Fractions of ethyl alcohol with b.p. 78° and propyl alcohol with b.p. 96-97° were used for the work.

The method of analysis of the liquid phase consisted in evaporation of a weighed sample, and ignition of the latter to constant weight. Our attention was directed to the development of a method for determining alcohols in the solid phases of heteropolyacid hydratoalcoholates. For this purpose we used the following procedure: In a separate sample of crystals the total oxide content was determined by ignition; the loss in weight represented the water and alcohol content. The amount of water was determined from the loss in weight of the crystalline acid on ignition, the amount of alcohol found being subtracted.

For alcohol determination we used a procedure based on oxidation of alcohols by potassium permanganate in an acid medium. New samples of the solid phase were taken for determination of alcohols. In accordance with the Kolthoff method of alcohol determination [5], 10 ml of 4 N H_2SO_4 , and an excess of potassium permanganate - 25 ml of 0.1 N solution - were added to 10 ml of 0.1 N ethyl alcohol solution.

After standing for a day, the excess permanganate in the solution being analyzed was titrated iodometrically; alcohol was determined from the quantity of reduced permanganate.

In order to check the suitability of the procedure under the conditions of our work, we performed experiments in the determination of known quantities of ethyl alcohol in the presence of phosphomolybdic, phosphotungstic, and other acids. It was found that phosphotungstic and silicotungstic acids do not react with the reducing

TABLE 1

Solubility of Strongly Dehydrated Phosphotungstic Acid in Alcohols at 20°

Solvent (alcohol)	Content of $H_7[P(W_2O_7)_6]$ in liquid phase (in %)	Comp. of solid phase (in %)			Formula of the hydratoalcoholate
		$H_7[P(W_2O_7)_6]$	water	alcohol	
Ethyl	84.62	95.05	1.5	3.45	$H_7[P(W_2O_7)_6] \cdot 2.5H_2O$ $2.2C_2H_5OH$
Propyl	79.72	82.78	1.30	15.92	$H_7[P(W_2O_7)_6] \cdot 2.5H_2O$ $9C_3H_7OH$

TABLE 2

Solubility of Strongly Dehydrated Silicotungstic Acid in Ethyl Alcohol

Content of $H_8[Si(W_2O_7)_6]$ (in %)	Comp. of solid phase (in %)			Formula of the hydratoalcoholate
	$H_8[Si(W_2O_7)_6]$	water	alcohol	
76.64	93.77	2.9	3.33	$H_8[Si(W_2O_7)_6] \cdot 5H_2O \cdot C_2H_5OH$

agent; therefore, the excess potassium permanganate solution was titrated iodometrically with the required accuracy in their presence, and the alcohol determination was reliable. In the presence of molybdc acids, as experiment showed, the excess potassium permanganate could not be titrated iodometrically, since the molybdenum is reduced in this case, and the solution turns blue. For back-titration of excess $KMnO_4$ in the presence of heteropolymolybdc acids, therefore, we used 0.1 N hydrogen peroxide solution, which does not reduce the Mo^{VI} anions of phosphomolybdc and silicomolybdc acids. The 0.1 N H_2O_2 standard solution was stabilized with sulfuric acid in the amount of 2 g/liter.

Control experiments showed that the amount of alcohol titrated was 97.6% on the average in the presence of 0.5-1.0 g of phosphomolybdc acid, and 98.75% in the presence of a like amount of silicomolybdc acid.

Investigation of the Solubility of Strongly Dehydrated Heteropolyacids in Ethyl Alcohol

The solubility was studied by the customary method in a water thermostat whose temperature did not vary more than $\pm 0.1^\circ$. Equilibrium was attained after mixing for 3-5 hours; samples of the liquid phase were taken with a pipet having a tip packed with glass wool. To sample the solid phase, the liquid phase was poured off, and the solid-phase sample was carefully pressed out with filter paper on a glass plate.

Experiments in solubility determination showed that dehydrated phosphomolybdc acid forms extremely viscous solutions with ethyl and propyl alcohols; no solid phase separated from these solutions even after prolonged standing. When the acid was added, the solution viscosity increased until a vitreous mass was formed. No crystals were found on microscopic examination of the viscous acid solution.

Dehydrated phosphotungstic acid also gave viscous solutions with alcohols; in this case, however, a solid phase separated after standing for 48 to 72 hours, and samples of it were taken for analysis; the viscosity of alcoholic phosphotungstic acid solutions was less.

Dehydrated silicomolybdc and silicotungstic acids also formed viscous solutions in alcohols; the behavior of these heteropolyacids was similar to that of phosphomolybdc and phosphotungstic acids. We were unable to isolate a solid phase from silicomolybdc acid solutions. Nevertheless, we succeeded in determining the solubility of silicotungstic acid.

The results of study of the solubility of dehydrated heteropolyacids are given in Tables 1 and 2.

TABLE 3

Equilibria in the Systems $H_7[P(Mo_2O_7)_6] \cdot 24H_2O$ and $H_7[P(W_2O_7)_6] \cdot 21H_2O$ - EtOH and PrOH

Temperature	Content of anhydrous acid in the liquid phase (in %)	Comp. of solid phase (in %)			No. of moles of H ₂ O or alcohol per mole of H ₇ [P(Mo ₂ O ₇) ₆] and H ₇ [P(W ₂ O ₇) ₆] in solid hydratoalcoholates		
		anhydrous acid	water of crystallization	alcohol	H ₂ O	C ₂ H ₅ OH	C ₃ H ₇ OH
Phosphomolybdic acid - ethyl alcohol							
0°	72.91	79.19	17.07	3.74	18.3	1.9	
10	73.45	79.21	17.09	3.70	18.4	1.9	
20	74.05	79.23	17.24	3.53	18.5	1.8	
30	74.64	79.22	17.6	3.50	18.6	1.8	
40	75.29	79.21	17.37	3.42	18.7	1.7	
Phosphomolybdic acid—propyl alcohol							
0°	70.9	76.11	17.79	6.10	19.12		1.9
10	71.67	76.40	17.61	5.91	19.02		1.9
20	72.30	77.70	17.53	4.77	18.80		1.5
30	72.72	77.70	17.51	4.79	18.80		1.5
40	72.97	77.65	17.62	4.73	18.70		1.5
Phosphotungstic acid—ethyl alcohol							
0°	78.16	86.99	10.89	2.12	18.84	0.88	
10	79.36	87.11	10.89	2.10	18.84	0.88	
20	80.44	87.34	10.84	1.82	18.80	0.75	
30	81.35	87.50	10.41	1.80	18.42	0.74	
40	82.09	88.22	10.01	1.76	18.30	0.72	
Phosphotungstic acid—propyl alcohol							
0°	76.14	86.66	9.53	3.81	15.88		2
10	77.40	86.50	9.94	3.63	15.88		2
20	78.70	86.50	10.94	2.56	18.50		1.5
30	80.03	86.54	10.92	2.50	18.50		1.5
40	81.30	86.68	10.91	2.41	18.50		1.4

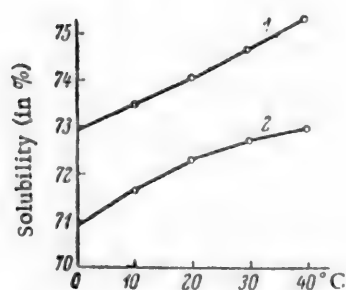


Fig. 1. Solubility of phosphomolybdic acid in EtOH (1) and PrOH (2).

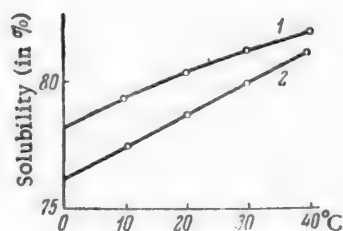


Fig. 2. Solubility of phosphotungstic acid in EtOH (1) and PrOH (2).

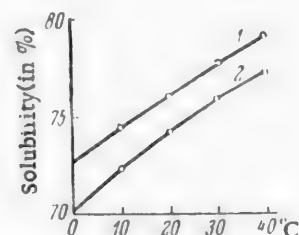


Fig. 3. Solubility of silicomolybdic acid in EtOH (1) and PrOH (2).

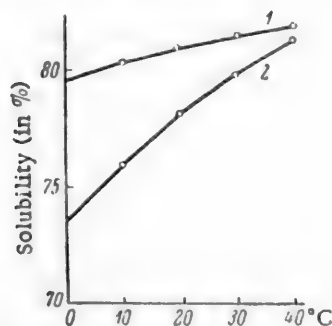


Fig. 4. Solubility of silicotungstic acid in EtOH (1) and PrOH (2).

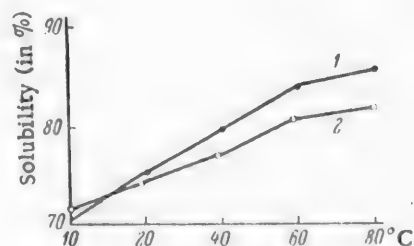


Fig. 5. Solubility of silicotungstic (1) and phosphotungstic (2) acids in isoamyl alcohol.

TABLE 4

Equilibria in the Systems $H_8[Si(Mo_2O_7)_6] \cdot 28H_2O$ and $H_8[Si(W_2O_7)_6] \cdot 26H_2O$ - Ethyl and Propyl Alcohols

Temperature	Content of anhydrous acid in the liquid phase (in %)	Comp. of solid phase (in %)			No. of moles of H ₂ O and an alcohol per mole of H ₈ [Si(Mo ₂ O ₇) ₆] and H ₈ [Si(W ₂ O ₇) ₆] in solid hydratoalcoholates		
		anhydrous acid	water of crystallization	alcohol	H ₂ O	C ₂ H ₅ OH	C ₃ H ₇ OH
Silicomolybdic acid— ethyl alcohol							
0°	72.69	78.49	20.11	1.40	21.85	1.0	
10	74.40	79.61	18.80	1.59	20.40	1.0	
20	76.10	80.37	17.49	2.14	19.01	1.0	
30	77.56	80.47	17.40	2.10	19.05	1.0	
40	79.02	80.58	17.37	2.05	19.00	1.0	
Silicomolybdic acid— propyl alcohol							
0°	70.2	78.18	20.42	1.40	22.55		0.4
10	72.3	79.51	18.21	2.11	19.79		0.7
20	74.18	81.04	16.03	2.93	17.53		1.0
30	75.82	81.06	16.05	2.91	17.56		1.0
40	77.15	81.10	16.07	2.81	17.56		1.0
Silicotungstic acid — ethyl alcohol							
0°	79.5	94.42	5.22	0.36	9	0.3	
10	80.33	94.21	5.71	0.35	9.8	0.3	
20	81.04	94.50	4.36	1.14	7.6	0.7	
30	81.16	94.91	4.35	1.15	7.6	0.7	
40	82.04	95.32	3.48	1.20	6.7	0.7	
Silicotungstic acid— propyl alcohol							
0°	73.49	93.16	5.54	1.21	9.5		0.6
10	76.02	93.45	5.01	1.30	8.63		0.6
20	78.20	93.71	4.27	2.02	7.5		1.0
30	80.02	93.91	4.08	2.00	7.03		1.0
40	81.56	92.98	4.12	1.90	7.03		1.0

From the data of Tables 1 and 2 it is evident that phosphotungstic and silicotungstic acids are readily soluble in alcohols; phosphotungstic acid is more soluble in ethyl alcohol than in propyl alcohol.

Owing to the fact that the investigation of the dehydrated acids was greatly hindered by the prolonged settling time of the solid phase and the high viscosity of the solutions, the solubility of the heteropolyacids was not determined at other temperatures. For the further systematic study of solubility in alcohols, nondehydrated heteropolyacid preparations were used.

Equilibria in Systems with Nondehydrated Heteropolyacids

In these investigations sampling required great attention and skill, owing to the high solubility of the heteropolyacids and volatility of the solvents.

On preparing alcoholic solutions of hydrated heteropolyacids we did not observe the formation of such viscous systems as those encountered earlier in the study of equilibria with dehydrated preparations. Equilibrium was established within 2-2.5 hours; the settling time was 2-3 hours. We studied the solubility of the heteropolyacids in the 0-40° temperature range. The results of study of the solubility of heteropolyacids with a phosphorus complex-former are given in Table 3 and Figs. 1 and 2.

From the data of Table 3 and Figs. 1 and 2, it follows that: 1) phosphotungstic acid is more soluble in alcohols than phosphomolybdic acid; 2) phosphomolybdic and phosphotungstic acids are more soluble in ethyl

TABLE 5

Equilibria in the Systems $H_7[P(W_2O_7)_6] \cdot 16H_2O$ and $H_8[Si(W_2O_7)_6] \cdot 18H_2O$ - Isoamyl Alcohol

Temp.	Content of anhydrous acid in the liquid phase (%)	Comp. of solid phase (in %)			No. of moles of H ₂ O and an alcohol per mole of H ₇ [P(W ₂ O ₇) ₆] and H ₈ [Si(W ₂ O ₇) ₆] in solid hydratoalcoholates	
		anhydrous acid	water of crystallization	alcohol		
Phosphotungstic acid						
0°	71.33	87.9	9.06	3.04	15.1	1.2
20	74.10	88.10	7.79	4.11	13	1.5
40	77.33	88.24	5.66	6.10	10.5	2.3
60	81.04	88.34	4.76	6.90	8.7	2.5
80	82.12	90.3	1.78	7.92	2.96	3.0
Silicotungstic acid						
0°	70.54	87.87	8.54	3.59	14.2	1.3
20	75.13	87.91	7.24	4.85	12.2	2.0
40	79.60	88.18	6.13	5.60	10.2	2.0
60	84.45	90.10	3.60	6.30	6.0	2.3
80	86.26	92.60	0.48	6.92	1.0	2.5

TABLE 6

Solubility of Heteropolyacids in Acetone and Ethyl Ether at 20°

Original compound	Content of anhydrous acid in the liquid phase (in %)	
	acetone solution	ethereal solution
$H_8[Si(Mo_2O_7)_6] \cdot 26 H_2O$	75	71.52
$H_8[Si(W_2O_7)_6] \cdot 18 H_2O$	80.95	74.3
$H_7[P(W_2O_7)_6] \cdot 15.5 H_2O$	82.55	77.63
$H_7[P(Mo_2O_7)_6] \cdot 13.5 H_2O$	—	71.98

alcohol than in propyl alcohol; 3) the solubility of the acids increases with temperature; in this case, a slight change in the composition of the solid phases is observed; the small breaks in the solubility curves correspond to this.

The results of determination of the solubility of nondehydrated silicomolybdic and silicotungstic acids in ethyl and propyl alcohols are given in Table 4.

On the basis of the data of Table 4 and Figs. 3 and 4, it may be concluded that these heteropolyacids also are more soluble in ethyl alcohol than in propyl alcohol, silicotungstic acid being more soluble than silicomolybdic

acid. The solubility of the heteropolyacids increases quite markedly with temperature. In this case, the composition of the solid phase changes, the amount of water of hydration decreasing; the alcohol content in the hydratoalcoholate changes slightly.

Solubility of Phosphotungstic and Silicotungstic Acids in Isoamyl Alcohol

The isoamyl alcohol which we used was distilled beforehand and had b.p. 129°. We studied the solubility of phosphotungstic and silicotungstic acids in isoamyl alcohol at 0-80°.

Preliminary experiments showed that equilibrium in the indicated systems is established within 3 hours. The liquid phase was analyzed for its total oxide content. The solid phase was analyzed for its total oxide, water, and isoamyl alcohol contents. Isoamyl alcohol was determined permanganatometrically by the procedure given above.

Results of the solubility study are given in Table 5.

Study of the solubility of phosphotungstic and silicotungstic acids in isoamyl alcohol shows that in this case the amount of water of hydration in the solid phases decreases more rapidly with increase of temperature than in the case of solution in ethyl or propyl alcohol. Owing to this, the breaks in the solubility curves of both heteropolyacids are more pronounced (Fig. 5).

The alcohol content in the solid phase varies within narrow limits: 1.2 to 3 moles for phosphotungstic acid and 1.3 to 2.5 moles for silicotungstic acid.

The solubility of heteropolyacids in acetone and ether is also higher than in water, the solubility in acetone being higher than in ethyl ether. Phosphotungstic acid is more soluble in acetone than in ethyl alcohol. Experimental data are given in Table 6.

SUMMARY

1. The solubility of strongly dehydrated phosphotungstic and silicotungstic heteropolyacids in ethyl alcohol was determined at 20°. Similar experiments with heteropolymolybdic acids could not be performed, owing to the extremely high viscosity of alcoholic solutions of the indicated compounds.

2. The solubility of nondehydrated phosphotungstic, phosphomolybdic, silicotungstic, and silicomolybdic acids in ethyl and propyl alcohols between 0 and 40° was studied.

3. Hydratoalcoholates, containing various amounts of water and 1-2 moles of an alcohol, were isolated as solid phases.

4. The solubility of phosphotungstic and silicotungstic acids in isoamyl alcohol between 0 and 80° was studied.

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ELECTROREDUCTION OF VETIVONE AT THE DROPPING-MERCURY CATHODE IN MEDIA WITH DIFFERENT pH VALUES

E. V. Zobov and V. A. Tsiplyakova

Moldavian Scientific Research Institute of the Food Industry

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The quantity of the sesquiterpene ketone, vetivone, contained in vetiver oil is one of the important characteristics of this essential oil, which is used in perfumery. In order to study the possibilities of separate determination of vetivone in vetiver oil, we conducted a polarographic investigation of vetivone, using a background

* See C.B. translation.

of ammonium chloride and hydrochloric acid [1], which showed that vetivone could be determined polarographically under the stated conditions.

The purpose of the present work is to ascertain the pH range in which polarographic determination of vetivone is possible, and also to study the mechanism of electroreduction of vetivone at the dropping-mercury cathode.

EXPERIMENTAL

The polarographic investigation of vetivone was conducted by means of a visual polarographic assembly with a GZS-47 galvanometer having a sensitivity of 10^{-9} amp/mm, provided with a shunt which reduced the sensitivity to $1/200$ of the maximum value. Two dropping-mercury electrodes, whose respective capillary characteristics were: 1) $m^{2/3}t^{1/6} = 3.86 \text{ mg}^{2/3} \text{ sec}^{-1/2}$; 2) $m^{2/3}t^{1/6} = 2.44 \text{ mg}^{2/3} \text{ sec}^{-1/2}$, were used as cathode. The anode was a saturated calomel electrode, separated by an agar-agar bridge from the solution being polarographed. A temperature of $25 \pm 0.5^\circ$ was maintained in the thermostatted polarographic cell. Before taking each polarogram, electrolytic hydrogen was passed for 15 min through the solution being polarographed. As background, 70% alcoholic-aqueous buffer solutions with pH values from 1.2 to 9.0 were used. Hydrochloric acid buffer mixture was used for pH 1-2, citrate mixture for pH 2.6-8, and alkali-borate mixture for pH 8-10. The pH values of the indicated solutions were checked by means of an LP-5 pH meter provided with a glass electrode.

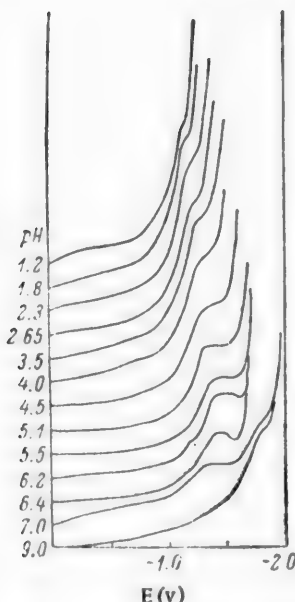


Fig. 1. Polarographic waves of vetivone at different pH values.

The vetivone which we used for the investigation was isolated from the essential oil of *Vetiveria zizanioides* and had the following constants: b.p. 120° (0.1 mm), d^{20}_4 1.004 and n^{20}_D 1.526, corresponding to literature data for vetivone [2,3]. As a result of the experiments, we found that in media with pH values of 1.2-5.5, vetivone was reduced at the dropping-mercury electrode, forming a one-step wave (Fig. 1), whose half-wave potential became ever more negative as the pH increased. In media with pH values from 6.2 to 9.0, vetivone was reduced, forming a two-step wave. The second steps of the waves

for pH 6.2 and 6.4 had a small maximum. At pH 9.0 the first step was very faint, so that the half-wave potential could not be determined.

The relation between concentration and diffusion current was determined by polarographing five concentrations of vetivone from 2.95 to 13.69 millimolar for each pH value. Since it was necessary to use two capillaries in the course of the work, the relation of diffusion current to concentration is expressed through the quantity

$K = \frac{i_d}{Cm^{2/3}t^{1/6}}$, which does not depend on the capillary characteristic. The relation of the diffusion current to pH is shown in Fig. 2. The sum of the diffusion currents of the first and second steps was used in constructing the graph. As is evident from the data given, the total diffusion current remained essentially unchanged in the pH interval 1.2-3.5, decreased as the pH rose from 3.5 to 7, and then began to increase. We found the half-wave potentials of vetivone graphically. Up to the appearance of the second step, a linear relation was maintained between the half-wave potential and the pH (Fig. 3), which is expressed by the equation $\frac{\Delta E_{1/2}}{\Delta \text{pH}} = 0.056 \text{ v}$.

The half-wave potential of the second step was essentially independent of the pH (table).

The polarographic waves of vetivone conformed to the equation $E = E_{1/2} + \frac{0.0591}{\alpha} \lg \frac{i}{i_d - i}$, where values of α , found from the slope of the straight lines $\lg \frac{i}{i_d - i} - E$, vary from $\alpha = 0.33$ to 0.63 as the pH varies from 1.2 to 5.5; this indicates an irreversible process in the given case.

In the pH interval from 6.2 to 9, $\alpha = 0.48$ for the first step. For the second step, $\alpha = 0.85$, which is close to unity and indicates a reversible, one-electron stage in the process occurring in the second step of reduction.

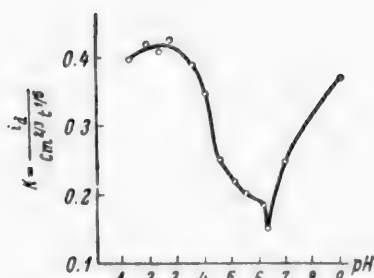


Fig. 2. Relation between the diffusion current of vetivone and pH.

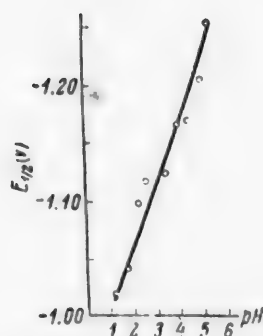


Fig. 3. Relation between $E_{1/2}$ for vetivone and pH.

Relation Between $E_{1/2}$ for Vetivone and pH

pH	$E'_{1/2}$	$E''_{1/2}$
1.2	-1.020	—
1.8	-1.041	—
2.3	-1.098	—
2.65	-1.117	—
3.5	-1.124	—
4.0	-1.166	—
4.5	-1.170	—
5.1	-1.205	—
5.5	-1.253	—
6.2	-1.113	-1.330
6.4	-1.22	—
7.0	-1.111	-1.651
9.0	—	-1.64

According to the data of [2], two-step reduction at the dropping-mercury cathode may be due to a different mechanism of hydrogen addition. In acid media the reduction goes according to the mechanism:

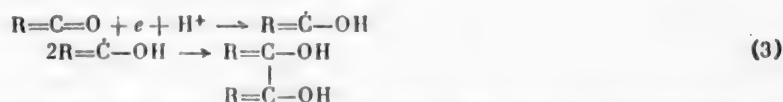


In alkaline media it goes according to the mechanism:



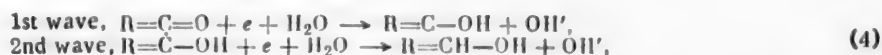
At pH values from 4.5 to 6.5, both processes may occur simultaneously. It is further stated that in the case where the process goes by mechanism (1), a functional relation between $E_{1/2}$ and pH is observed; when it goes by mechanism (2), however, this functionality is less marked, or even completely absent.

In the literature there are also numerous data regarding the mechanism of electrochemical conversion of carbonyl compounds which, with the exception of certain carbonyl-containing compounds having a double bond conjugated with the carbonyl group [7], are reduced to alcohols (two-electron mechanism) or glycols (one-electron mechanism) [3-6]. Taking into account the two-step, two-electron reduction of vetivone in alkaline media, which excludes the possibility of the reduction mechanism considered in the case of ketones with conjugated double bonds [7], as well as the fact that in acid and neutral media vetivone may also be reduced by the two-electron mechanism, we believe it most probable that the electroreduction of vetivone in media with a pH from 1.2 to 6.4 goes according to the following equations:



This process causes the formation of the first steps of the vetivone waves and leads to the formation of a glycol.

The appearance of a second step on the vetivone polarogram at a pH between 6.2 and 9 is due, in our opinion, to a process taking place according to the equations:



with the formation of an alcohol. At a pH from 6.2 to 6.5, the first wave may be formed as the result of a process conforming to mechanism (3).

The stated conclusions are also confirmed by the fact that at a pH from 1.2 to 5.5 a linear relation between $E_{1/2}$ and pH is observed for the first step, but not for the second.

The relation between the diffusion current and pH also confirms the assumed mechanism of the process. As is evident from Fig. 2, the current strength diminishes as the hydrogen-ion concentration decreases, owing to the slackening of process (3), and then increases with the rise of process (4).

In conclusion, we consider it our duty to thank Yu. S. Lyalikov for valuable advice.

SUMMARY

1. The polarographic properties of vetivone were investigated in media with different pH values.
2. The relations of $E_{1/2}$ and i_d to pH for vetivone were studied.
3. Possible mechanisms of the electroreduction of vetivone at the dropping-mercury electrode are given.

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STUDY OF THE PROCESS OF ALKALINE OXIDATION OF ISOPROPYLBENZENE.

ON THE MECHANISM OF ALKALINE INITIATION OF THE REACTION

V. A. Simanov and M. S. Nemtsov

S. V. Lebedev All-Union Scientific Research Institute of Synthetic Rubber
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The oxidation of alkylbenzene hydrocarbons and, in particular, isopropylbenzene, by molecular oxygen for the purpose of preparing valuable chemical products has been the objective of numerous investigations. In the first works in this field [1,2], however, there are generally no indications of the presence of peroxides in the oxidation products. Isopropylbenzene hydroperoxide was isolated and studied for the first time in 1943 by R. Yu. Udris,* who oxidized sufficiently pure isopropylbenzene over very small amounts of manganese catalyst, thus proving the possibility of carrying out the process with only slight decomposition of the hydroperoxide. The first report in foreign literature was that of Hock and Lang [4], who isolated the hydroperoxide from the oxidation products of pure isopropylbenzene irradiated with ultraviolet light.

*Cited in [3].

TABLE 1

Characteristics of Isopropylbenzene Samples

	No. of sample and alkylation catalyst	
	I AlCl ₃	II H ₃ PO ₄ on kieselguhr
d_4^{20}	0.860	0.861
n_D^{20}	1.4910	1.4910
Boiling range		
Beginning of boiling	150.1°	150.9°
Boiling range of 10-90% fraction	150.5-151.3°	151.4-152.4°
End of boiling	153.0°	153.5°
Iodine number	0.04	1.17

In the oxidation of isopropylbenzene, emulsified in aqueous sodium carbonate solution [5], an extremely pure hydrocarbon, specially purified by hydrogenation to a methylstyrene content less than 0.005%, was also used.

Other authors [6] showed that by preliminary treatment of isopropylbenzene with certain substances, especially concentrated sulfuric acid, the rate of oxidation could be sharply increased. Without mentioning other works and patents, described in review articles [7], it should be noted that in all published works on the oxidation of isopropylbenzene for the purpose of preparing its hydroperoxide a product of high purity was used.

The possibility of using lower quality isopropylbenzene without special preliminary purification was first shown in works [8] on the oxidation of isopropylbenzene in the presence of caustic alkali. The latter process was realized in α -methylstyrene production [9, 14]. However, notwithstanding the industrial use of the alkali method of isopropylbenzene oxidation, a number of questions connected with the peculiarities of this process remained obscure. The purpose of the present work was to fill this gap to some extent. Two samples of technical isopropylbenzene, prepared by different industrial methods of benzene alkylation by propylene, were used in the work. The first sample (I) was the product obtained on alkylation in the liquid phase at low temperature in the presence of aluminum chloride catalyst. The second sample (II) was obtained through the vapor-phase alkylation of benzene by propylene at high temperatures and pressures in the presence of phosphoric acid on kieselguhr.

The characteristics of these samples, given in Table 1, show that they differ sharply in their content of unsaturated compounds. The increased unsaturation of the sample alkylated over phosphoric acid is the result of higher working concentrations of propylene in the reaction zone of this process; this leads to the development of side reactions of olefin polymerization.

The isopropylbenzene was oxidized by atmospheric oxygen in a reaction vessel consisting of a glass cylinder of about 100 ml capacity, with a sealed-in, porous glass filter and an electrically heated jacket. Boiling toluene (110°) was used as heat carrier. A diagram of the setup, which is similar to that described earlier [10, 11] is shown in Fig. 1. In order to carry out the oxidation in the kinetic region, the air feed rate was maintained at 12 liters/hour per 60 ml of isopropylbenzene charge. The degree of oxidation of isopropylbenzene was followed by means of the change in the refractive index of the reaction mass, and calculated by the formula: $X = 0.298 \times \Delta n_D^{20} \cdot 10^4$, where X is the content of oxidation products (in mole %), which may be regarded as equal to the total degree of isopropylbenzene conversion, and Δn_D^{20} is the difference between the refractive indices of the reaction liquid and isopropylbenzene.

The use of this method is based on the fact that the refraction coefficients of the main decomposition products of isopropylbenzene hydroperoxide - dimethylphenylcarbinol, acetophenone - as well as that of the hydroperoxide itself, are very nearly the same.

The isopropylbenzene hydroperoxide content α (in wt.%) was determined iodometrically by titrating a sample with 0.1 N thiosulfate solution [5, 16]. The degree of decomposition β of the initially formed

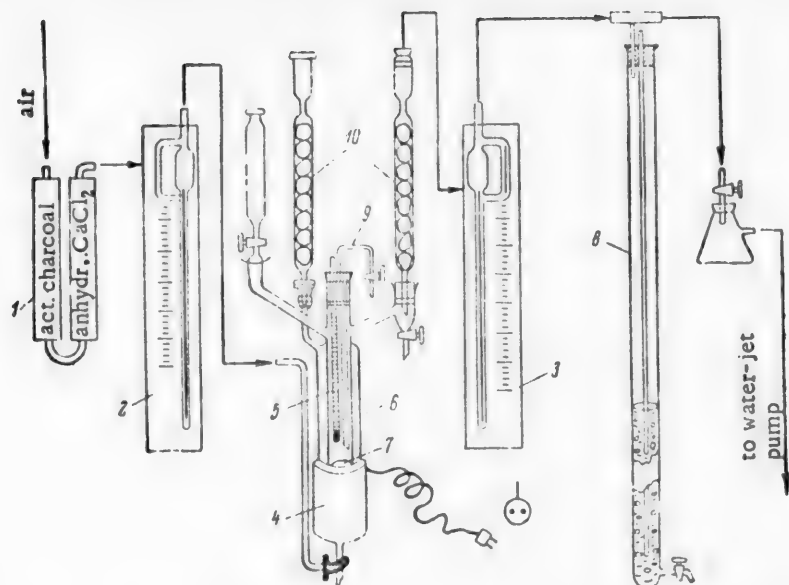


Fig. 1. Diagram of the setup for isopropylbenzene oxidation: 1) air purifier; 2) and 3) flowmeters; 4) electric heater; 5) thermometer; 6) jacket; 7) No. 1 porous filter; 8) manostat; 9) sample-takeoff tube; 10) condensers.

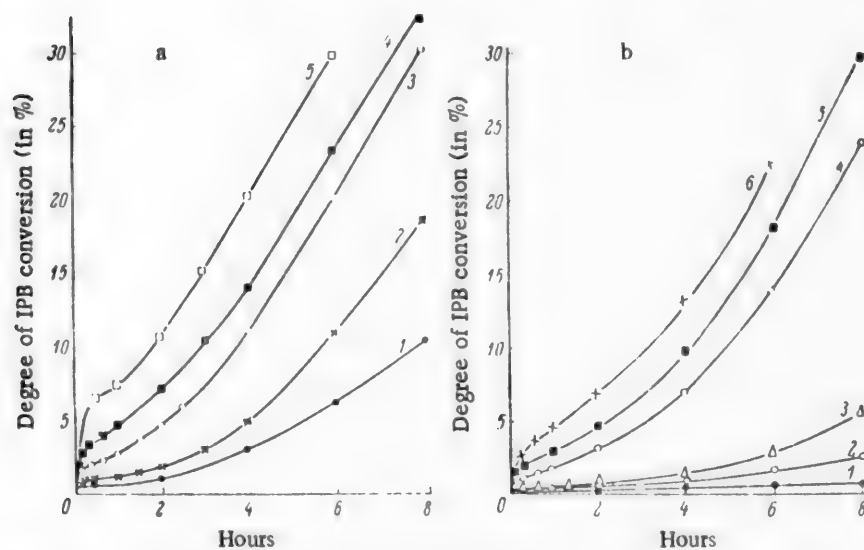


Fig. 2. a. Effect of the amount of sodium hydroxide on the rate of oxidation of isopropylbenzene I: 1) nothing added; 2) 0.01% NaOH; 3) 0.05% NaOH; 4) 0.10% NaOH; 5) 0.50% NaOH. b. Effect of the amount of sodium hydroxide on the rate of oxidation of isopropylbenzene II: 1) nothing added; 2) 0.01% NaOH; 3) 0.025% NaOH; 4) 0.05% NaOH; 5) 0.10% NaOH; 6) 0.20% NaOH.

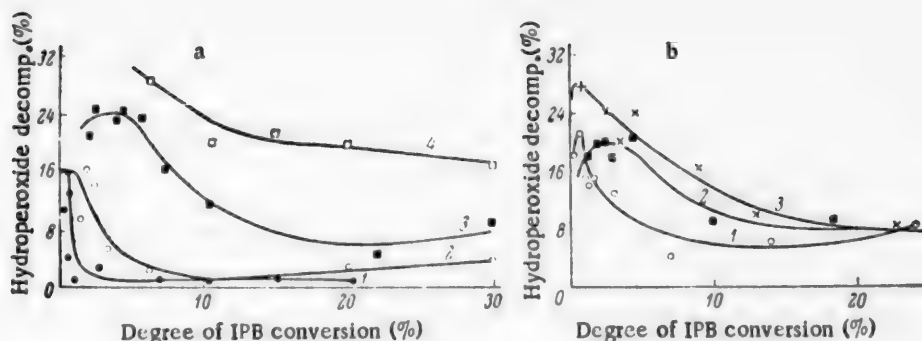


Fig. 3. **a.** Effect of the amount of sodium hydroxide on the decomposition of isopropylbenzene I hydroperoxide in the process of its oxidation: 1) 0.01% NaOH; 2) 0.05% NaOH; 3) 0.10% NaOH; 4) 0.50% NaOH. **b.** Effect of the amount of sodium hydroxide on the decomposition of isopropylbenzene II hydroperoxide in the process of its oxidation: 1) 0.05% NaOH; 2) 0.10% NaOH; 3) 0.20% NaOH.

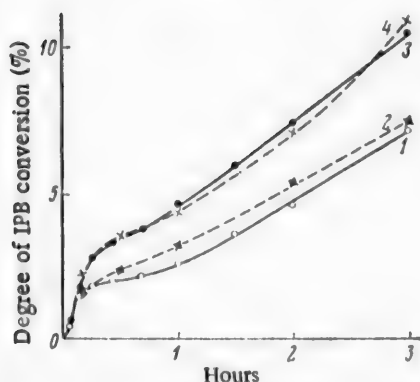


Fig. 4. Kinetics of oxidation of isopropylbenzene I in the presence of bis-isobutyric acid azodinitrile and alkali: 1) 0.05% NaOH; 2) 0.05% diniz; 3) 0.10% NaOH; 4) 0.10% diniz.

hydroperoxide was calculated by the formula: $\beta = \frac{x-y}{x} \cdot 100\%$, where $y = \frac{3.75 \cdot a}{4.75 - 0.01a}$ is the hydroperoxide content (in mole %), calculated from analytical data for **a** (in wt.%).

The error of determination of β grows when the degree of hydroperoxide decomposition is appreciably increased, but in the region of slight decomposition satisfactory accuracy of measurement is obtained.

At the beginning of the work the refraction coefficient n_D^{20} was determined by means of a refractometer of the Abbe type, generally used for control in isopropylbenzene hydroperoxide production, which gave a variance $\Delta n_D^{20} = \pm 0.0002$ in different measurements; this leads to an error of about 1% in the determination of the degree of oxidation. In subsequent experiments, however, where it was necessary to study the character of the initial stage of the process more precisely, an IRF-23 (Pulfrich-type) refractometer was used; this permitted an approximately tenfold increase in the accuracy of determination.

In experiments in the alkaline oxidation of isopropylbenzene, 0.4-1.0 wt% of isopropylbenzene hydroperoxide was added to the latter beforehand. This "priming" permitted a sharp decrease in the length of the induction period usual for hydrocarbon autoxidation. The kinetic curves, given in Fig. 2 for both isopropylbenzene samples, show that free caustic alkali substantially affects the rate of oxidation. Thus, addition of caustic alkali causes a steep rise of the kinetic curve at the very beginning of the reaction, the height of this rise increasing regularly with the quantity of alkali. The difference in the initial stage of the process for different isopropylbenzene samples consists only in the fact that the height of the jump in kinetic curves obtained with a given quantity of caustic alkali is about twice as great for the purer product I as for sample II. In the following oxidation period the reaction rate is a more complex function of the quantity of alkali. Thus, on addition of 0.05% or more of NaOH the branches of the curves after 3-4 hours of oxidation have practically the same slope for both isopropylbenzene samples. With smaller quantities of alkali a different oxidation rate is observed throughout the entire experiment. In this case, the less pure isopropylbenzene sample II, which practically is not oxidized at all in the absence of alkali, reacts very slowly even in the presence of 0.025% NaOH, while the final rate for sample I approximates the maximum even with 0.01% NaOH. The differences found in the character of the effect of small amounts of alkali on the oxidation of isopropylbenzene samples I and II are apparently due to the presence therein of different amounts of harmful admixtures, in the binding of whose conversion products different amounts of alkali are consumed.

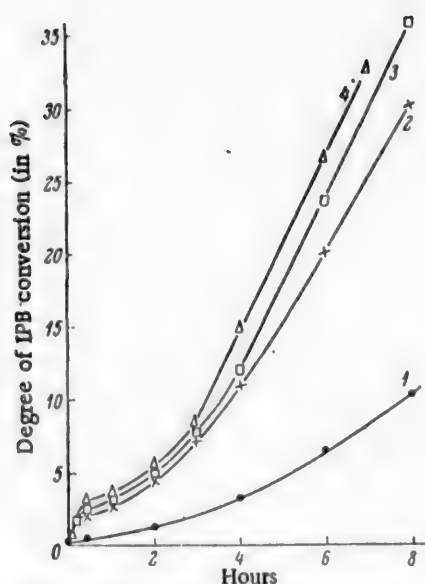


Fig. 5. Oxidation kinetics of isopropylbenzene I in the presence of equivalent quantities of NaOH and Na_2CO_3 : 1) nothing added, Expt. 134; 2) Na_2CO_3 (equiv. to 0.05% NaOH), Expt. 130; 3) 0.05% NaOH, Expt. 135.

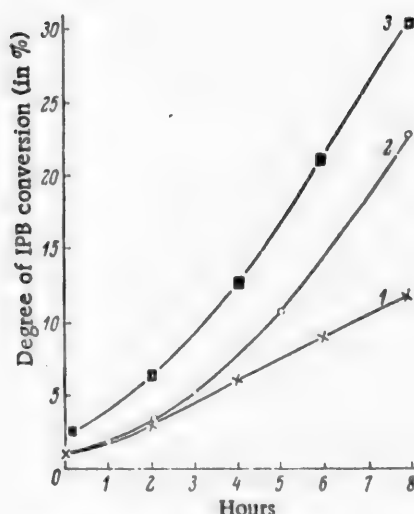


Fig. 6. Oxidation kinetics of isopropylbenzene I in the presence of equimolar quantities of RbOH, KOH, and NaOH: 1) nothing added, Expt. 76; 2) NaOH (0.05 wt.%), Expt. 72; 3) KOH (equiv. to 0.05% NaOH), Expt. 70; 4) RbOH (equiv. to 0.05% NaOH), Expt. 66.

In the light of current concepts [12], the chain reaction of oxidation is initiated by free radicals formed in the decomposition of the hydroperoxide. In conformity with this, the sharp increase in the reaction rate in the initial period of isopropylbenzene oxidation in the presence of caustic alkali should be due to an increase in the free-radical concentration as a result of acceleration of the radical decomposition of isopropylbenzene hydroperoxide by alkali. This conclusion is in accord with the curves of variation of the degree of isopropylbenzene hydroperoxide decomposition with respect to the degree of conversion for the same experiments (Figs. 3a and 3b), which show that at the beginning of the oxidation the reaction rate is higher, and the degree of hydroperoxide decomposition is greatly increased.

Finally, this conclusion is confirmed by the closeness of the kinetic curves of isopropylbenzene oxidation under the usual conditions of the alkali process, and on initiation of the reaction by addition to the isopropylbenzene of bis-isobutyric acid azodinitrile (diniz), which rapidly decomposes at 60–70° to form free radicals [13]. In experiments with diniz, hydroperoxide "priming" was not used.

Experimental kinetic curves (Fig. 4) in both cases indicate the identity of the character of initiation of the reaction by free radicals. Thus, when the reaction is initiated by diniz, the latter, being practically completely decomposed in the first 10–15 min, leads to a sharp increase in the free-radical concentration, which makes for a high reaction rate in this period. When the diniz is used up, the chain reaction is maintained only through the thermal decomposition of isopropylbenzene hydroperoxide itself into radicals, the rate of which is relatively low. This transition from one source of initiation to another is reflected in the kinetic curves in the form of breaks.

A 100% increase in the quantity of diniz does not change the character of the process, but the height of rise of the curve, up to the break point, increases in this case. The absence of direct proportionality between the height of the "jump" in the curve and the quantity of diniz obviously is due to the increase in the rate of recombination of free radicals on increase of their concentration. On the basis of the fully analogous character of the curves in Fig. 4 for the alkali oxidation process, it may be assumed that, in this case, decomposition of isopropylbenzene hydroperoxide into free radicals under the influence of caustic alkali occurs mainly in the initial period of oxidation, during which the alkali is bound by acid byproducts of the reaction; after it is almost completely

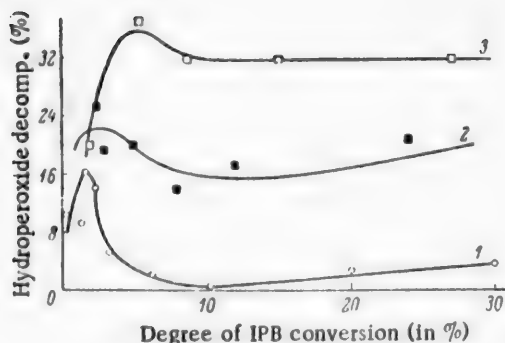
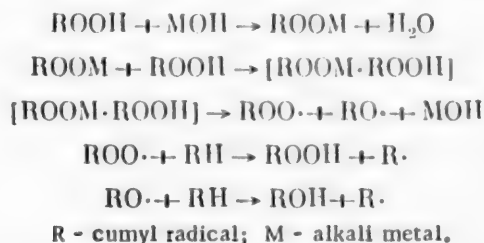


Fig. 7. Effect of RbOH, KOH, and NaOH on the decomposition of isopropylbenzene I hydroperoxide in the process of its oxidation: 1) NaOH, Expt. 72; 2) KOH, Expt. 70; 3) RbOH, Expt. 66.

the light of the conclusions reached above that the excess alkali promotes an increase in the rate of hydroperoxide decomposition in the initial oxidation period, and simultaneously leads to increased formation of acid by-products (e.g., benzoic acid). In this case, correspondingly, a greater amount of alkali is consumed in binding them, and in the subsequent periods of oxidation free alkali is practically absent in all cases.

Turning to the mechanism of the effect of free alkali on the initiation of isopropylbenzene oxidation, we must point out that, in earlier works [8], intermediate formation of the sodium salt of isopropylbenzene hydroperoxide in the alkali process of oxidation was assumed; the latter also decomposed into free radicals. Later [15], it was experimentally shown that the anhydrous sodium salt of the hydroperoxide can form a complex with the free hydroperoxide, of the type $\text{ROONa} \cdot \text{ROOH}$ (where ROOH is isopropylbenzene hydroperoxide, and ROONa is its salt), which has much less thermal stability than the hydroperoxide salt itself.

On the basis of these data the mechanism of initiation of isopropylbenzene oxidation in the presence of caustic alkali may be represented by the following reaction scheme:



Thus, according to the proposed scheme, caustic alkali is regenerated in the process of initiation and, hence, is a typical catalyst of the process. In the actual process, however, as was mentioned above, the alkali is gradually consumed, being bound by acid products of side-reactions.

As was shown by analysis of the salts precipitated in industrial reaction columns on carrying out the technical process of alkaline oxidation of isopropylbenzene, they consist largely of sodium carbonate. Since the latter, being characterized by a high pH, can also have a favorable effect on the oxidation process [5], direct experiments were performed, the results of which are presented graphically in Fig. 5, where kinetic curves for the oxidation of pure isopropylbenzene without admixture, with added alkali, and with added soda are also shown for comparison. Consideration of these curves shows that soda, like caustic alkali, leads to considerable acceleration of the process in time, i.e., by binding the acid byproducts of the reaction, it makes possible an increase in the oxidation rate as a result of a rise in the concentration of free radicals, the rate of formation of which is proportional to the hydroperoxide content in the reaction liquid, which increases with time. Contrary to caustic alkali, however, soda does not give an initial jump in the curve; hence, it may be concluded that soda cannot initiate the radical decomposition of isopropylbenzene hydroperoxide. The reason for this difference should be sought in the fact that soda, being a salt of a stronger acid than the hydroperoxide, cannot form the hydroperoxide sodium salt required to activate the process.

used up, the process continues, as in the case of initiation by diniz, through the thermal decomposition of the hydroperoxide. From this point of view, the above-mentioned difference in the effect of the amount of alkali on the oxidation of isopropylbenzene of different degrees of purity is understandable. Thus, in the case of sample II, which has more harmful impurities (see Fig. 2b), 0.025% of NaOH was not enough to bind the reaction byproducts, as a result of which the initial "jump" in the reaction rate was not observed at all; the latter remained very low throughout the experiment. In the case of the purer sample I, as was mentioned above, about half as much alkali was required in order to bind the reaction byproducts, which inhibited the process. On the basis of the virtual constancy, mentioned in the discussion of Fig. 2, of the reaction rate on increase of the quantity of alkali over 0.05%, it may be inferred in

TABLE 2

Effect of the Nature of the Caustic Alkali

	Alkali cation		
	Na	K	Rb
Ionic radius according to Pauling, r	0.95	1.33	1.48
Initial rise in the hydroperoxide content (after 12 min) Δ HP, in mole %	1.6	2.0	2.7
Ratio Δ HP/ r	1.7	1.5	1.8

Since the rate of decomposition of the complex mentioned above may depend substantially on the nature of the cation in the hydroperoxide salt, it could be expected that replacement of sodium hydroxide by other hydroxides would lead to different oxidation rates. This hypothesis is confirmed by the experimental data given in Figs. 6 and 7. Thus, when equivalent quantities of the hydroxides of different Group I metals are introduced, the observed effect increases in the order from Na to Rb; the extent of their influence is proportional to the ionic radius (see Table 2).

Consideration of the curves in Fig. 7 also shows that potassium and rubidium cause a sharp increase in the amount of isopropylbenzene hydroperoxide decomposition products; on this basis one may conclude that the technical use of sodium hydroxide is preferable in practice.

SUMMARY

1. The role of caustic alkali in the alkaline oxidation of isopropylbenzene is not limited to binding acid byproducts of the reaction, but consists also in activation of the radical decomposition of isopropylbenzene hydroperoxide.
2. The character of alkaline initiation of the oxidation process is the same as in the case of generation of free radicals by thermal decomposition of bis-Isobutyric acid azodinitrile.
3. The rate of initiation of isopropylbenzene oxidation substantially depends on the nature of the caustic alkali.
4. On the basis of the experimental data obtained, a probable scheme for the mechanism of the alkaline oxidation of isopropylbenzene is proposed.

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SYNTHESIS OF SOME DICHLORO DERIVATIVES OF 2,6-OCTADIENE

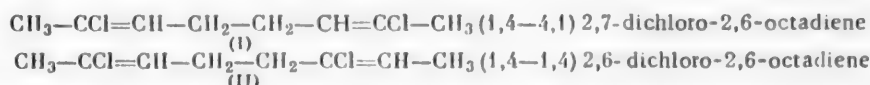
A. L. Klebanskii and V. F. Vosik

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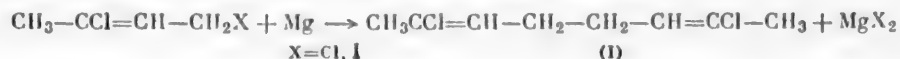
Original article submitted June 15, 1959

Dichloro derivatives of 2,6-octadiene are of considerable interest as model systems for studying the complex chemical processes occurring in polychloroprene. The polychloroprene molecule is mainly built up of chloro-2-butene units, connected in the 1,4-1,4 positions. At the same time, we cannot exclude the possibility of some units being connected in the 1,4-4,1 positions. As the nature of reactions occurring in high-molecular and low-molecular compounds is the same in principle, and the only difference is the fact that the reactions are slower in polymers due to the high viscosity of the latter, it is advantageous to study the reactivity of chloroprene rubber on systems simulating its structure and consisting of two polymer units connected in the 1,4-1,4 and 1,4-4,1 positions.

In the present communication, we present a method of synthesizing two compounds simulating the main types of possible structures of chloroprene rubber.



Both compounds were synthesized for the first time, and the first was obtained from 1,3-dichloro-2-butene (III) or from 1-iodo-3-chloro-2-butene (IV) by organomagnesium synthesis.



1,3-Dichloro-2-butene (III) undergoes organomagnesium synthesis very slowly, and only with magnesium that has been well activated with iodine at a high temperature (150°). As the reactivity of the halide increases with a change from chlorine to iodine, the organomagnesium synthesis was carried out with 1-iodo-3-chloro-2-butene (IV). The latter has not been described previously, and it was synthesized by two methods; namely, the addition of HI (gas) to chloroprene in glacial acetic acid, and the exchange of compound (III) with NaI or KI in acetone (preferably NaI, as its solubility in acetone is considerably higher than that of KI).

Six isomers are possible from the organomagnesium synthesis, depending on the order of coupling of the units. By chemical methods and infrared spectral data we demonstrated that the reaction products contained only compound (I), as it was established that saponifiable chlorine was absent, there were two chlorine atoms present on a carbon atom with a double bond, and there were no side vinyl groups or conjugation of the double bonds.

For the synthesis of 2,6-dichloro-2,6-octadiene (II) we started from 2,6,8-trichloro-2,6-octadiene, $\text{CH}_3-\text{CCl}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CCl}=\text{CH}-\text{CH}_2\text{Cl}$ (V), which was obtained by condensation of 1,3-dichloro-2-butene

with chloroprene in the presence of anhydrous FeCl_3 [1]. Various reduction methods, both with atomic hydrogen and catalytic methods, were tried for the conversion of 2,6,8-trichloro-2,6-octadiene into compound (II). Complete reduction of the saponifiable chlorine atom without a change in unsaturation was achieved by hydrogenation in the presence of Raney nickel and CH_3COONa to bind the hydrogen chloride. The structure of the 2,6-dichloro-2,6-octadiene obtained by this method was established by infrared spectral data.

EXPERIMENTAL

1,3-Dichloro-2-butene (III). was isolated from the still residues from the synthesis of chloroprene, and purified by repeated distillation; it had b.p. $127-129^\circ$ at 760 mm, d^{20}_4 1.1590, n^{20}_D 1.4698, which corresponds to literature data [2].

Found %: Cl (sapon.) 28.1. $\text{C}_4\text{H}_6\text{Cl}_2$. Calculated %: Cl (sapon.) 28.4.

The NaI and KI were recrystallized from alcohol and dried to constant weight. Anhydrous acetone was used.

1-Iodo-3-chloro-2-butene (IV). Into a three-necked flask with a reflux condenser and a stirrer were placed 120 g of NaI and 1 liter of acetone. Over a period of 4 hr, 350 g of (III) was added from a dropping funnel with heating of the mixture to 50° and vigorous stirring for 3 hr, and then the acetone solution was carefully separated from the precipitate of NaCl or KCl, the acetone removed by distillation on a water bath, and the residual product washed three times successively with 10% hyposulfite solution and distilled water, dried over baked MgSO_4 , and vacuum distilled. The b.p. was 70° at 18 mm. The yield was 50%. The substance was very unstable, decomposed continuously with the liberation of iodine, and its physicochemical constants for different samples were insufficiently reproducible, especially for samples that had been stored.

B.p. 70° at 18 mm, n^{20}_D 1.5714, d^{20}_4 1.8200.

Found %: I (sapon.) 58.0. M 219.3. $\text{C}_4\text{H}_6\text{ClI}$. Calculated %: I (sapon.) 58.6. M 216.5.

The synthesis of (IV) by the reaction of chloroprene with HI (gas) was carried out under the same conditions as for the reaction of chloroprene with HBr [3]. HI (gas) was obtained from tetralin and crystalline iodine [3].

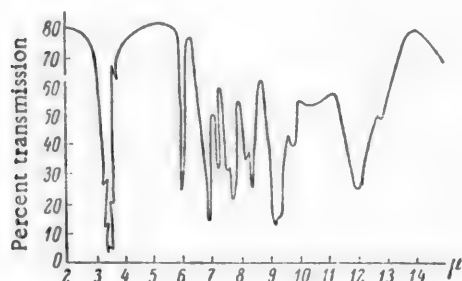


Fig. 1. Infrared spectrum of 2,7-dichloro-2,6-octadiene.

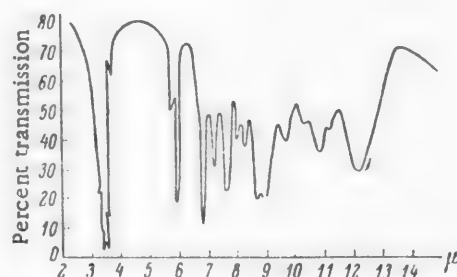


Fig. 2. Infrared spectrum of 2,6-dichloro-2,6-octadiene.

2,7-Dichloro-2,6-octadiene (I). Into a three-necked flask with a dropping funnel, condenser, stirrer, and thermometer was placed 2 g of magnesium turnings, which were then covered with absolute ether. A solution of 26 g of freshly distilled 1-iodo-3-chloro-2-butene (IV) in three times the volume of absolute ether was added gradually from the dropping funnel. The reaction began vigorously after the addition of a few drops of the ether solution and the reaction mixture was cooled in an ice bath. After the reaction had finished, the mixture was stirred for 3-4 hr with the ether boiling and then decomposed with 10% NH_4Cl solution acidified with HCl or 10% CH_3COOH . The ether layer was separated, washed with distilled water, and dried over baked MgSO_4 . The ether was removed and the product vacuum distilled.

B.p. 78° at 10 mm, n^{20}_D 1.4830; d^{20}_4 1.0566. There was no saponifiable chlorine; unsaturation, 94%.

Found %: Cl (total) 39.5. M 177.4. $\text{C}_8\text{H}_{12}\text{Cl}_2$. Calculated %: Cl (total) 39.9, M 179.

2,6-Dichloro-2,6-octadiene. For the synthesis of this compound we used freshly distilled 2,6,8-trichloro-2,6-octadiene. The constants corresponded to literature data [1]. Into a long-necked hydrogenation flask were placed 10 g of the starting material, 4 g of CH_3COONa in 20 ml of H_2O , 20 ml of alcohol, and 4.8 g of Raney nickel. Hydrogen was obtained by the action of 35% NaOH on aluminum with subsequent purification of the gas by passage through KMnO_4 solution. The hydrogenation was carried out by vigorous shaking of the flask at room temperature. The reaction was followed by the amount of hydrogen absorbed. At the end of the reduction, the product was salted out with Na_2CO_3 , the alcohol removed by distillation, and the distillation residue washed with water, dried over baked MgSO_4 , and vacuum distilled. The yield was 25%.

B.p. 73° at 10 mm; n_D^{20} 1.4680; d_4^{20} 1.0108; unsaturation 96%.

Found %: Cl (total) 39.4. M 174.5. $\text{C}_8\text{H}_{12}\text{Cl}_2$. Calculated %: Cl (total) 39.9, M 179.

Infrared spectra* were plotted to establish the structures of compounds (I) and (II). The general form of the absorption curves for 2,7- and 2,6-dichloro-2,6-octadienes are given in Figs. 1 and 2. For determination of structural characteristics, the frequencies of valence and deformation vibrations of hydrogen atoms, and also the double-bond frequencies, are of the greatest interest. In the region of C-H valence vibrations ($3500\text{--}2800\text{ cm}^{-1}$), both compounds showed five frequencies (3020, 2978, 2950, 2920, and 2855 cm^{-1}), which indicate the presence of CH_3 , CH_2 , and CH groups. The absence of an absorption band close to 3100 cm^{-1} for 2,6-dichloro-2,6-octadiene (II) indicates the absence of a structure of the type $-\text{CH}=\text{CH}_2$ or $>\text{C}=\text{CH}_2$ [4]. In the region of C=C frequencies, the compounds investigated showed the frequency 1670 cm^{-1} , which is characteristic of the grouping $\text{R}_1\text{R}_2\text{C}=\text{CHR}_3$. Among the C-H deformation frequencies (planar), there were well-expressed frequencies at 1450 and 1382 cm^{-1} , confirming the presence of CH_2 and CH_3 groups. The absence of absorption close to $1412\text{--}1430\text{ cm}^{-1}$ indicates the absence of a CH_2 group. For the groups of frequencies of planar vibrations, there was a strong band close to 830 cm^{-1} (826 cm^{-1}), indicating that 2,7-dichloro-2,6-octadiene (I) has a structure of the $\text{R}_1\text{R}_2\text{C}=\text{CHR}_3$ type. All these data indicate the absence of conjugation, and confirm the structures of the compounds obtained.

SUMMARY

1. We synthesized 2,7- and 2,6-dichloro-2,6-octadienes, which simulate the structures of chloroprene polymers with the units linked in the 1,4-4,1 and 1,4-1,4 positions.
2. The structures of the compounds obtained were demonstrated by chemical methods and by infrared spectroscopy.

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* The infrared spectra were plotted and interpreted by G. I. Semenov.

** Original Russian pagination. See C. B. Translation.

BENZAZOLES

2-HYDRAZINO- AND 2-AZIDOBENZIMIDAZOLES*

N. P. Bednyagina and I. Ya. Postovskii

Ural Polytechnic Institute

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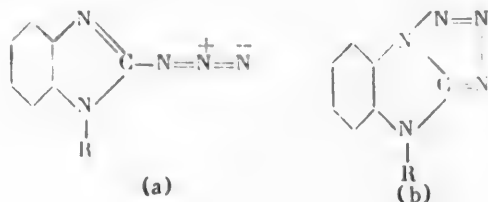
Original article submitted June 1, 1959

We previously synthesized 2-hydrazino derivatives of benzazoles (2-hydrazinobenzimidazole, 2-hydrazinobenzthiazole, and 2-hydrazinobenzoxazole), and studied the action on blood pressure of these compounds as their water-soluble hydrochlorides [1].** Of these compounds, only 2-hydrazinobenzimidazole was found to be active, but, in contrast to 1-hydrazinophthalazine ("apresoline") [2], a known preparation which reduces blood pressure, 2-hydrazinobenzimidazole increases the blood pressure of animals. On this basis, and also considering the special interest in benzimidazole derivatives due to the successful use of 2-benzylbenzimidazole ("dibazol") in medical practice [3], we continued the investigation of 2-hydrazinobenzimidazole derivatives.

In contrast to 2-hydrazinobenzimidazole (IV), which increases blood pressure, and also in contrast to inactive 1-methyl-2-hydrazinobenzimidazole (V), 1-benzyl-2-hydrazinobenzimidazole hydrochloride (VI), which was synthesized for testing, considerably reduces the blood pressure of animals. Compounds in which there is an additional methyl group in the ring, 5(6)-methyl-1-benzyl-2-hydrazinobenzimidazole, show an even stronger hypotensive action. In connection with the observed physiological action, it seemed interesting to study the substances obtained in more detail.

Hydrazino derivatives of benzimidazole have not been studied much chemically. There are only patent data [4] for 2-hydrazinobenzimidazole. We started with the synthesis of 2-hydrazinobenzimidazole and its N-alkyl derivatives from 2-chlorobenzimidazole [5]. This compound and its N-alkyl derivatives were converted into the corresponding hydrazines by heating in sealed tubes with hydrazine hydrate. 5-Methylbenzimidazoles were obtained analogously from 5-methyl-3-chlorobenzimidazole. In the preparation of 5(6)-methyl-1-benzyl derivatives, two isomers were not observed and the position of the methyl group remained undetermined. All the 1-alkyl-2-hydrazinobenzimidazoles were unstable; in the form of free bases, they rapidly became blue and resinified in air in the presence of moisture. Alcohol solutions of them rapidly became dark violet and on standing they deposited beautiful black-violet crystals with a metallic green luster. The structure of these compounds has not been studied up to now. Only unsubstituted 2-hydrazinobenzimidazole could be stored for an unlimited period in the form of the crystalline base, but alcohol solutions of it slowly became colored on standing. The hydrochlorides of all the hydrazinobenzimidazoles were stable. Like hydrazinophthalazine [2], 2-hydrazinobenzimidazoles form hydrazones with difficulty. Thus, we obtained the benzaldehyde hydrazone of 2-hydrazinobenzimidazole only by carrying out the reaction in a sealed tube at 150°.

In studying the chemical reactions and conversions of 2-hydrazinobenzimidazoles it seemed interesting to study, among other reactions, their reaction with nitrous acid. In this case one might expect the formation of 2-azido derivatives (a) or tetrazolobenzimidazoles (b).



*Presented at the Eighth Mendeleev Conference, Moscow, March, 1959.

**The pharmacological testing of all the compounds obtained previously, and those described in the present article, was carried out by I. F. Panov (Pharmacology Department, Sverdlovsk Medical Institute).

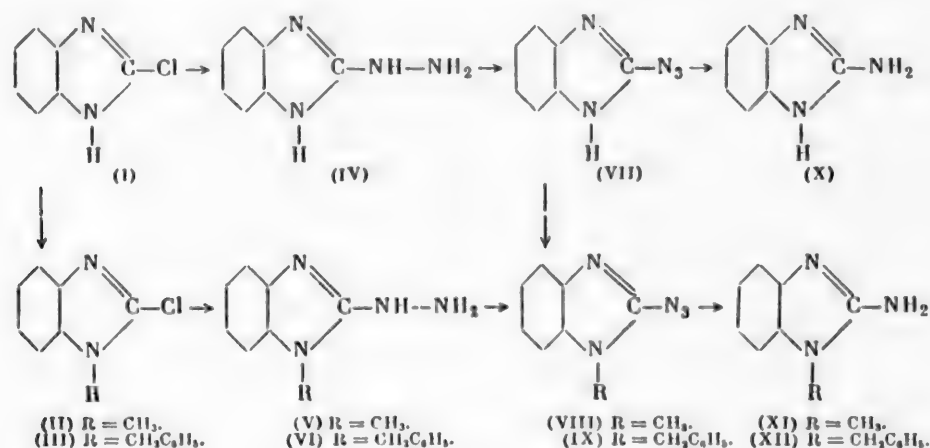
By the action of potassium nitrite on aqueous solutions of the hydrazine hydrochlorides or of sodium nitrite on solutions of the hydrazine bases in acetic acid, we obtained stable, crystalline, though light-sensitive substances. The compounds obtained from hydrazines that were not substituted at the nitrogen ($R = H$) crystallized readily from polar solvents and were not soluble in hydrocarbons. They formed readily hydrolyzable sodium salts and could be alkylated with alkyl halides in alkali solution. Compounds alkylated at the nitrogen ($R = CH_3$; $CH_2C_6H_5$) crystallized from hydrocarbons and had lower melting points.

The structures of the compounds obtained were determined by the study of the infrared spectra. They all had clear absorption bands characteristic of azides [6,7] with the first at $2100-2200\text{ cm}^{-1}$ (asymmetric valence vibrations) and the second at $1200-1300\text{ cm}^{-1}$ (symmetric valence vibrations). For most of them, the peaks were double (see Table 1).

A chemical demonstration of the azide structure of the compounds obtained was the ease of their reduction to amines. Azides may be reduced with various reducing agents [8]. In the present work we reduced azides with Raney nickel in anhydrous alcohol at room temperature for the first time, as far as we know.* The reduction gave an almost quantitative yield of the amine (Table 2) and, in some cases, could be used for preparing amines, starting from the hydrazines, or served as the main method for analyzing azides.

Thus, the action of nitrous acid on 2-hydrazinobenzimidazoles formed azides, but not tetrazoles. According to literature data [8,9], in a number of cases, hydrazines of six-membered heterocycles containing the grouping $-N = C - NH - NH_2$ are converted to tetrazoles by the action of nitrous acid, but hydrazines of five-membered heterocycles (azoles) containing the same grouping give azides. The results of our work again confirm this observation and indicate that it is a rule.

The synthesis based on 2-chlorobenzimidazole achieved in the present work are shown in the scheme. The same conversions were achieved for 5-methyl-2-chlorobenzimidazole.



EXPERIMENTAL

2-Hydrazinobenzimidazole (IV). A mixture of 24 g of 2-chlorobenzimidazole (m.p. $210-212^\circ$ [5]) and 100 ml of hydrazine hydrate was heated at $150-155^\circ$ for 4 hr in sealed tubes. After the tubes had been opened, the crystalline 2-hydrazinobenzimidazole was collected by filtration and washed with water. The yield was 18.6 g (80%). The m.p. was $219-220^\circ$ (from alcohol) ($221-222^\circ$ [4]). On standing, an alcohol solution gradually acquired a violet color. The hydrochloride crystallized from water or alcohol. It contained water of crystallization and the hydrate melted at $65-67^\circ$. After being dried at 105° , the compound had m.p. $185-186^\circ$. By heating 2-hydrazinobenzimidazole with excess benzaldehyde in a sealed tube at 150° for 4 hr, we obtained a quantitative yield of the hydrazone with m.p. $270-272^\circ$ (from alcohol).

Found %: N 23.43. $C_{14}H_{12}N_4$. Calculated %: N 23.72.

* An authentic tetrazole, tetrazolophthalazine, which was obtained from 1-hydrazinophthalazine and sodium nitrite (according to [2]), was unchanged under these conditions.

TABLE 1

Azidobenzimidazoles

Substance	Name	Empirical formula	Melting point	% N		Infrared absorption bands ^{••} ascribed to azido group			
				found	calc.	in crystals ^{•••}		in benzene solution	
						2100-2200 cm ⁻¹	1300-1300 cm ⁻¹	2100-2200 cm ⁻¹	1300-1300 cm ⁻¹
(VII)	2-Azidobenzimidazole	C ₇ H ₅ N ₅	188-189° *	44.35	44.01	2190 (w) 2130 (s)	1263 (s) 1221 (av)	2125 •••••	•••••
(VIII)	1-Methyl-2-azidobenzimidazole	C ₈ H ₇ N ₅	87-88	40.39	40.44	2175 (w) 2120 (s)	1285 (av) 1267 (av)	2165 (av) 2130 (s)	1282 (w) 1236 (w)
(IX)	1-Benzyl-2-azidobenzimidazole	C ₁₄ H ₁₁ N ₅	108-110	28.28	28.10	2180 (w) 2137 (s)	1282 (av) 1268 (w) 1247 (w)	2130 (s)	1282 (av) 1247 (w)
(VIIa)	5-Methyl-2-azidobenzimidazole	C ₈ H ₇ N ₅	184-185 *	40.37	40.44	2122 (s)	1279 (s) 1222 (w)	2122 •••••	•••••
(IXa)	5(6)-Methyl-1-benzyl-2-azidobenzimidazole	C ₁₅ H ₁₃ N ₅	122-124	26.38	26.60	2191 (w) 2122 (s)	1289 (s) 1264 (s)	2130 (s)	1282 (s) 1265 (av) 1247 (av)

• Decomposition point.

•• IKS-12 instrument. NaCl prism.

••• In a paste with a perfluorinated hydrocarbon or in vaseline oil.

•••• Band not observed due to low solubility of substance in benzene.

TABLE 2

2-Aminobenzimidazoles

Substance	Name	Empirical formula	Melting point	Recrystallization solvent	% N	
					found	calc.
(X)	2-Aminobenzimidazole	C ₇ H ₇ N ₃	222° (222 [13])	Water	31.57	31.56
(XI)	1-Methyl-2-amino-benzimidazole	C ₈ H ₉ N ₃	200—201	Water	28.43	28.55
(XII)	1-Benzyl-2-amino-benzimidazole	C ₁₄ H ₁₃ N ₃	192—193	Benzene or alcohol	19.09	18.82
(XIa)	5-Methyl-2-amino-benzimidazole	C ₈ H ₉ N ₃	196—197	Water	28.52	28.55
(XIIa)	5(6)-Methyl-1-benzyl-2-amino-benzimidazole	C ₁₅ H ₁₅ N ₃	215—216	Diluted alcohol	17.84	17.71

1-Methyl-2-hydrazinobenzimidazole (V). To a solution of 10 g of 2-chlorobenzimidazole in 10 ml of 30% NaOH was added 30 ml of methyl iodide and 20 ml of alcohol. After being boiled for 1 hr, the mixture was diluted with water. The yield of 1-methyl-2-chlorobenzimidazole was 8 g (73%). The m.p. was 114–115° (from dilute alcohol). The reaction with hydrazine hydrate was carried out as above. The yield of 1-methyl-2-hydrazinobenzimidazole was 75–77% and the m.p. 146–147°. The moist crystals rapidly turned violet in air. Treatment with 2 N HCl yielded the hydrochloride with m.p. 293–295° (from water).

Found %: N 28.21. C₈H₁₀N₄ · HCl. Calculated %: N 28.03.

1-Benzyl-2-hydrazinobenzimidazole (VI). To a solution of 20 g of 2-chlorobenzimidazole in 20 ml of 30% NaOH were added 100 ml of alcohol and 40 ml of benzyl chloride. After it had been boiled for 1 hr, the mixture was diluted with water to liberate an oily emulsion, which crystallized on cooling. The yield of 1-benzyl-2-chlorobenzimidazole was 28 g (90%). The m.p. was 108–109° (from dilute alcohol).

Found %: N 11.71. C₁₄H₁₁N₂Cl. Calculated %: N 11.54.

The reaction with hydrazine hydrate was analogous to (IV). Freshly prepared 1-benzyl-2-hydrazinobenzimidazole had m.p. 140–145°.

Found %: N 23.65. C₁₄H₁₄N₄. Calculated %: N 23.51.

The substance rapidly began to turn violet and resinify in air. An alcohol solution gradually turned inky violet and deposited coarse needles (up to 1 cm long) with a green metallic luster.

The hydrochloride of the hydrazine was stable and had m.p. 75–80° (from water, hydrate). After being dried above 100°, it had m.p. 230–233°.

Found %: N 20.51; C 61.60; H 5.22. C₁₄H₁₄N₄ · HCl. Calculated %: N 20.39; C 61.26; H 5.50.

5-Methyl-2-hydrazinobenzimidazole (IVa). 3-Nitro-4-aminotoluene with m.p. 114–115° (115° [10]) was reduced with zinc dust in an alkaline alcohol medium analogously to the reduction of o-nitroaniline [11]. 3,4-Diaminotoluene was isolated as the hydrochloride by evaporation of the acidified filtrate. 3,4-Diaminotoluene hydrochloride was fused with one equivalent of urea and after the vigorous reaction, the melt was dissolved in dilute alkali and the solution acidified to precipitate 5-methyl-2-benzimidazolone with m.p. 302–304° (299–301° [12]). The latter was heated with phosphorus oxychloride in sealed tubes at 160–165° for 3 hr. We obtained 5-methyl-2-chlorobenzimidazole with m.p. 176–180 (from alcohol) in 80% yield.

Found %: N 16.84. C₈H₇N₂Cl. Calculated %: N 16.81.

Heating in sealed tubes with hydrazine hydrate [analogous to (IV)] yielded crystalline 5-methyl-2-hydrazinobenzimidazole with m.p. 180–182° (from dilute alcohol).

Found %: N 34.29. $C_8H_{10}N_4$. Calculated %: N 34.55.

The hydrochloride was hygroscopic and crystallized with difficulty.

5(6)-Methyl-1-benzyl-2-hydrazinobenzimidazole (VIa). 5-Methyl-2-chlorobenzimidazole (5 g) was dissolved in 5 ml of 30% NaOH and boiled for 1 hr with 10 ml of benzyl chloride in 25 ml of alcohol. Dilution with water precipitated an oil, which crystallized on standing in the cold. The yield of 5(6)-methyl-1-benzyl-2-chlorobenzimidazole was 4.5 g (70%). The m.p. was 120-121° (from alcohol).

Found %: N 10.69. $C_{15}H_{13}N_2Cl$. Calculated %: N 10.91.

The chloride obtained was heated in a sealed tube with hydrazine hydrate [analogous to (IV)]. 5(6)-Methyl-1-benzyl-2-hydrazinobenzimidazole was obtained as a thick, colorless, honeylike resin, which was insoluble in water and rapidly became blue in air. The hydrochloride was stable and had m.p. 215-218° (from water).

Found %: N 19.38. $C_{15}H_{16}N_4 \cdot HCl$. Calculated %: N 19.41.

2-Azidobenzimidazole (VII). 2-Hydrazinobenzimidazole (3.0 g) was dissolved in glacial acetic acid (20 ml) at room temperature and water (40 ml) added. A solution of 1.7 g of $NaNO_2$ in 10 ml of water was added to the solution at 3-5°. An almost colorless crystalline precipitate of the azide formed rapidly on stirring. The yield was 3 g (94%). The product formed coarse platelets from dilute alcohol. 2-Azidobenzimidazole was readily soluble in alcohol and 2 N NaOH (it gave a readily hydrolyzable crystalline sodium salt). It was difficultly soluble in benzene, ether, and chloroform. On standing in light, the compound became brown on the side facing the light.

5-Methyl-2-azidobenzimidazole (VIIa) and 5(6)-methyl-1-benzyl-2-azidobenzimidazole (IXa) were obtained analogously (see Table 1).

1-Methyl-2-azidobenzimidazole (VIII). A solution of 2 g of 1-methyl-2-hydrazinobenzimidazole in 20 ml of water was cooled to 3-5° and a solution of 2 g of KNO_2 in 10 ml of water added. There was slight heat evolution and a yellowish crystalline precipitate of the azide formed immediately. The yield was 2.5 g (98%). The m.p. was 87-88° (from dilute alcohol; soft, fibrous needles). The methylated compound (VII) could also be obtained: 0.8 g of 2-azidobenzimidazole was boiled with a solution of 10 ml of alcohol, 3 ml of CH_3I , and 4 ml of 2 N NaOH for 1 hr (or in alkaline solution with 5 ml of dimethyl sulfate). Dilution with water and cooling gave a quantitative yield of 1-methyl-2-azidobenzimidazole. The m.p. was 85-88° (undepressed by the sample described above). The substance melted to a colorless liquid and decomposed vigorously when heated above 120°. It was readily soluble in organic solvents and became brown in light.

1-Benzyl-2-azidobenzimidazole (IX) was obtained analogously (see Table 1).

2-Aminobenzimidazoles (Table 2). 2-Azidobenzimidazoles (2-3 g) were dissolved in anhydrous alcohol (30-50 ml) at room temperature and 15-20 g of Raney nickel paste (stored under anhydrous alcohol) added. A reaction occurred with liberation of gas bubbles and slight evolution of heat (up to 40°). When visible reaction had ceased, the mixture was left for 1-2 hr. The nickel was removed by filtration and washed with anhydrous alcohol. Removal of the alcohol gave an almost quantitative yield (90-95%) of the corresponding 2-aminobenzimidazoles.

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SUMMARY

1. We synthesized 2-hydrazino derivatives of benzimidazole containing substituents at the nitrogen of the heterocycle (methyl and benzyl) and in the benzene ring (5-methyl). Some of these (N-benzyl derivatives) showed a hypotensive action.

2. The action of nitrous acid on 2-hydrazinobenzimidazole and its derivatives substituted in the benzimidazole ring gave azides, and tetrazoles were not formed.

3. The azides were reduced by Raney nickel at room temperature to give amines.

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UNSYMMETRICAL DERIVATIVES OF

1,6-DIARYLHYDRAZODITHIODICARBAMIDES. I.

R. G. Dubenko and P. S. Pel'kis

Institute of Organic Chemistry, Academy of Sciences of the UkrSSR

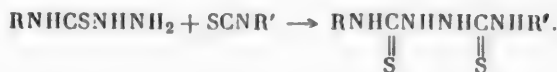
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Compounds with interesting physiological properties have recently been found among substituted thiocarbonylides, phenylthiosemicarbazides, and 1,4-diphenylthiosemicarbazides [1,2]. It seemed interesting to synthesize and study various unsymmetrical 1,6-diphenylhydrazodithiodicarbamides with the general formula $RNHCSNHNHCSNHR'$, which are similar to them in properties. This series of compounds has been investigated very little [3]. Apparently, they should be oxidizable at the hydrazo bond, react in the thiol form, and form complexes with various cations. These compounds are also interesting in that they cyclize comparatively readily into derivatives of thiourazoles.

The derivatives of 1,6-diarylhydrazodithiocarbamide were obtained by the reaction of substituted 4-phenylthiosemicarbazides with the appropriate substituted phenyl isothiocyanates in hot anhydrous alcohol according to the scheme:



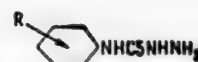
The synthesis of some substituted 4-phenylthiosemicarbazides from the corresponding mustard oils and hydrazine hydrate in an alcohol medium has been described in the literature [4]; however, by this method the compounds were obtained in low yields and they were difficult to isolate in a pure form. The derivatives of 4-phenylthiosemicarbazide given in Table 1 were obtained from the corresponding substituted phenyl isothiocyanates and hydrazine hydrate in aqueous alcohol [5].

In their turn, the substituted phenyl isothiocyanates were synthesized from the corresponding amines and thiophosgene in chloroform and water [6]. The procedure for preparing the substituted phenyl isothiocyanates that have not been described in the literature is given in the experimental section.

*Original Russian pagination. See C.B. translation.

TABLE 1

4-Arylthiosemicarbazides with the General Formula



R	Melting point	Yield (in %)	Empirical formula	% N	
				found	calc.
o-n-C ₃ H ₇ O	88°	71	C ₁₀ H ₁₃ ON ₃ S	18.44, 18.57	18.67
p-n-C ₃ H ₇ O	170	68	C ₁₀ H ₁₃ ON ₃ S	18.81, 18.62	18.67
o-iso-C ₄ H ₉ O	75	80	C ₁₁ H ₁₇ ON ₃ S	17.26, 17.37	17.57
o-n-C ₄ H ₉ O	81	85	C ₁₁ H ₁₇ ON ₃ S	17.61, 17.50	17.57
o-iso-C ₅ H ₁₁ O	108	88	C ₁₂ H ₁₉ ON ₃ S	16.51, 16.39	16.60
p-iso-C ₅ H ₁₁ O	159	90	C ₁₂ H ₁₉ ON ₃ S	16.30	16.60
p-C ₂ H ₅	159	87	C ₉ H ₁₃ N ₃ S	21.18, 21.34	21.54
p-(CH ₃) ₃ C	139	72	C ₁₁ H ₁₇ N ₃ S	18.61, 18.63	18.83
p-CH ₃ CO	149	73	C ₉ H ₁₁ ON ₃ S	19.72	20.09
p-C ₂ H ₅ COO	150	80	C ₁₀ H ₁₃ N ₃ S	17.37, 17.27	17.57
p-CH ₃ CONH	185	98	C ₉ H ₁₂ ON ₄ S	25.25	25.0
o-Br	158	96	C ₇ H ₆ N ₃ SB	16.89, 16.70	17.07
m-Br	103	80	C ₇ H ₆ N ₃ SB	17.45, 17.35	17.07
p-Br	180	75	C ₇ H ₆ N ₃ SB	16.97, 17.02	17.07
o-I	154	92	C ₇ H ₆ N ₃ SI	14.31, 14.44	14.33
m-I	136	65	C ₇ H ₆ N ₃ SI	13.96, 14.01	14.33
p-I	182	71	C ₇ H ₆ N ₃ SI	13.91	14.33
p-H ₂ NSO ₂	178	82	C ₉ H ₁₀ O ₂ N ₄ S ₂	22.66, 22.66	22.76

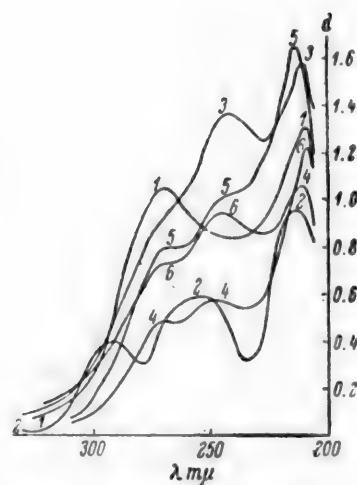


Fig. 1. Absorption curves of 4-phenylthiosemicarbazide derivatives in alcohol (solution concentration $6.6 \cdot 10^{-5}$ M): 1) 4-phenylthiosemicarbazide; 2) 4-(o-n-propoxyphenyl)-thiosemicarbazide; 3) 4-(p-n-propoxyphenyl)-thiosemicarbazide; 4) 4-(o-bromophenyl)-thiosemicarbazide; 5) 4-(m-bromophenyl)-thiosemicarbazide; 6) 4-(p-bromophenyl)-thiosemicarbazide.

Figures 1 and 2 show the ultraviolet absorption spectra of six derivatives of 4-phenylthiosemicarbazide and eight derivatives of 1,6-diphenylhydrazodithiocarbamide. The measurements were made with an SF-4 spectrophotometer on alcohol solutions. The absorption curves of the preparations in an aqueous alkali solution had only one maximum at 207-210 mμ (Fig. 3).

EXPERIMENTAL

p-Ethylphenyl isothiocyanate. A solution of 15 g of p-ethyl-aniline in 75 ml of chloroform was added with continuous stirring at a temperature no higher than 15° to a solution of 18.6 g of thiophosgene (12.4 ml) in 125 ml of water. Stirring was continued for a further hour; then the chloroform solution was separated and dried with calcium chloride. The chloroform was removed and the p-ethylphenyl isothiocyanate distilled. The b.p. was 113° at 4-5 mm. The yield was 17 g (85%).

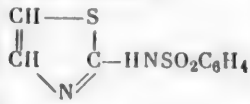
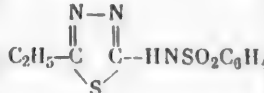
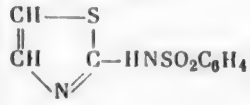
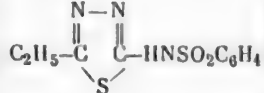
p-tert-Butylphenyl isothiocyanate. The reaction was carried out with 15 g of p-tert-butylaniline. We obtained 16 g (83%) of product with b.p. 126° at 4-5 mm.

4-(p-Ethylphenyl)-thiosemicarbazide. To an ice-cooled solution of 3.3 g of p-ethylphenyl isothiocyanate in 8 ml of alcohol was added 1.6 ml of 50% hydrazine hydrate in 5 ml of water, and the precipitate collected and recrystallized from alcohol. The 4-(p-ethylphenyl)-thiosemicarbazide formed white needles on recrystallization. The yield was 3.4 g.

4-(p-Acetophenyl)-thiosemicarbazide. The reaction was carried out with 1.6 ml of 50% hydrazine hydrate and 3.5 g of p-acetophenyl isothiocyanate. On recrystallization from alcohol, the product formed

TABLE 2

Unsymmetrical Derivatives of 1,6-Diphenylhydrazodithiodicarbamide with the General Formula $RNHCSNHNHCSNHR$; $R = C_6H_5$ (Nos. 1-23), $p-C_2H_5OC_6H_4$ (Nos. 24-39)

Sample No.	R'	Melting point	Yield (%)	Empirical Formula	% N	
					found	calc.
1	$p-CH_3OC_6H_4$	181°	98	$C_{15}H_{16}ON_4S_2$	16.69, 16.93	16.87
2	$o-C_2H_5OC_6H_4$	132	73	$C_{16}H_{18}ON_4S_2$	15.80, 15.81	16.18
3	$p-C_2H_5OC_6H_4$	188	65	$C_{16}H_{18}ON_4S_2$	15.82, 15.79	16.18
4	$p-iso-C_3H_7OC_6H_4$	180	88	$C_{17}H_{20}ON_4S_2$	15.57, 15.77	15.56
5	$o-n-C_3H_7OC_6H_4$	141	63	$C_{17}H_{20}ON_4S_2$	15.22, 15.39	15.56
6	$p-n-C_3H_7OC_6H_4$	183	55	$C_{17}H_{20}ON_4S_2$	15.72, 15.92	15.56
7	$o-iso-C_4H_9OC_6H_4$	133	89	$C_{18}H_{22}ON_4S_2$	14.63, 14.60	14.97
8	$o-n-C_4H_9OC_6H_4$	130	52	$C_{18}H_{22}ON_4S_2$	15.13, 15.23	14.97
9	$p-n-C_4H_9OC_6H_4$	178	89	$C_{18}H_{22}ON_4S_2$	14.62, 14.76	14.97
10	$o-iso-C_5H_{11}OC_6H_4$	142	50	$C_{19}H_{24}ON_4S_2$	14.05, 14.71	14.43
11	$p-iso-C_5H_{11}OC_6H_4$	178	97	$C_{19}H_{24}ON_4S_2$	14.33, 14.29	14.43
12	$p-C_2H_5C_6H_4$	182	56	$C_{16}H_{18}N_4S_2$	17.16, 17.21	16.97
13	$p-(CH_3)_2CC_6H_4$	187	92	$C_{16}H_{18}N_4S_2$	15.89, 15.98	15.64
14	$p-CH_3COC_6H_4$	217	93	$C_{16}H_{16}ON_4S_2$	15.90, 15.95	16.28
15	$o-BrC_6H_4$	157	97	$C_{14}H_{13}N_4S_2Br$	14.34, 14.44	14.70
16	$m-BrC_6H_4$	144	56	$C_{14}H_{13}N_4S_2Br$	14.73, 14.77	14.70
17	$p-BrC_6H_4$	154	94	$C_{14}H_{13}N_4S_2Br$	15.02, 15.03	14.70
18	$o-I C_6H_4$	144	95	$C_{14}H_{13}N_4S_2I$	12.91, 13.10	13.08
19	$m-I C_6H_4$	134	95	$C_{14}H_{13}N_4S_2I$	12.91, 12.82	13.08
20	$p-I C_6H_4$	158	93	$C_{14}H_{13}N_4S_2I$	13.42, 13.40	13.08
21	$p-H_2NSO_2C_6H_4$	206	99	$C_{14}H_{15}O_2N_5S_3$	18.50, 18.55	18.37
22		180	97	$C_{17}H_{16}O_2N_6S_4$	17.77, 17.82	18.1
23		169	60	$C_{18}H_{19}O_2N_7S_4$	19.58, 19.55	19.88
24	$o-CH_3C_6H_4$	169	46	$C_{17}H_{20}ON_4S_2$	15.35, 15.28	15.56
25	$p-CH_3C_6H_4$	186	46	$C_{17}H_{20}ON_4S_2$	15.56, 15.25	15.56
26	$2,4-(CH_3)_2C_6H_3$	180	56	$C_{18}H_{22}ON_4S_2$	14.71, 14.60	14.97
27	$o-n-C_3H_7OC_6H_4$	188	32	$C_{19}H_{24}O_2N_4S_2$	14.10, 13.93	13.86
28	$p-n-C_3H_7OC_6H_4$	188	56	$C_{19}H_{24}O_2N_4S_2$	13.79, 13.91	13.86
29	$p-iso-C_3H_7OC_6H_4$	194	47	$C_{19}H_{24}O_2N_4S_2$	13.51, 13.64	13.86
30	$o-iso-C_4H_9OC_6H_4$	128	95	$C_{20}H_{26}O_2N_4S_2$	13.38, 13.44	13.39
31	$o-n-C_4H_9OC_6H_4$	135	97	$C_{20}H_{26}O_2N_4S_2$	13.27, 13.25	13.39
32	$p-n-C_4H_9OC_6H_4$	189	98	$C_{20}H_{26}O_2N_4S_2$	13.61, 13.74	13.39
33	$o-iso-C_5H_{11}OC_6H_4$	189	63	$C_{21}H_{28}O_2N_4S_2$	12.99, 13.05	12.96
34	$p-iso-C_5H_{11}OC_6H_4$	192	73	$C_{21}H_{28}O_2N_4S_2$	12.84, 13.01	12.96
35	$o-C_2H_5C_6H_4$	151	82	$C_{18}H_{22}O_2N_4S_2$	14.06, 13.99	14.36
36	$m-ClC_6H_4$	178	78	$C_{16}H_{17}ON_4S_2Cl$	14.77, 14.62	14.72
37	$p-H_2NSO_2C_6H_4$	188	99	$C_{16}H_{20}O_3N_5S_3$	16.75, 16.71	16.47
38		188	90	$C_{19}H_{20}O_3N_6S_4$	16.89, 16.77	16.54
39		174	80	$C_{20}H_{23}O_3N_7S_4$	18.50, 18.42	18.25

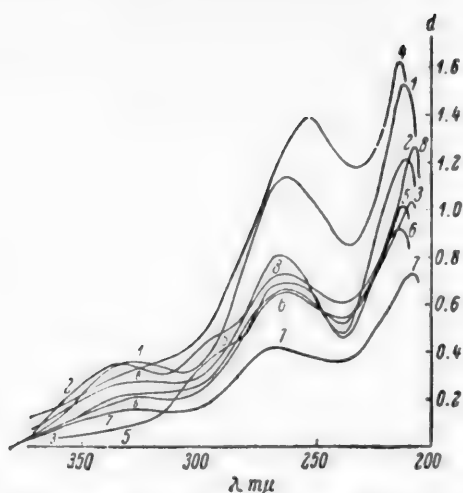


Fig. 2. Absorption curves of 1,6-diphenylhydrazodithiocarbamide derivatives in alcohol (solution concentrations: curves 1, 3, 4 - $3.3 \cdot 10^{-5}$ M; curve 2 - $2.2 \cdot 10^{-5}$ M; curves 5 and 6 - $1.32 \cdot 10^{-5}$ M): 1) 1,6-diphenylhydrazodithiocarbamide; 2) 1-phenyl-6-(o-phenetyl)-hydrazodithiocarbamide; 3) 1-phenyl-6-(p-phenetyl)-hydrazodithiocarbamide; 4) 1-phenyl-6-(o-n-propoxyphenyl)-hydrazodithiocarbamide; 5) 1-phenyl-6-(p-n-propoxyphenyl)-hydrazodithiocarbamide; 6) 1-phenyl-6-(o-bromophenyl)-hydrazodithiocarbamide; 7) 1-phenyl-6-(m-bromophenyl)-hydrazodithiocarbamide; 8) 1-phenyl-6-(p-bromophenyl)-hydrazodithiocarbamide.

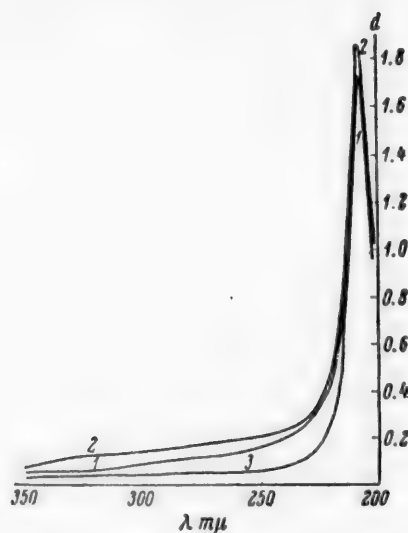


Fig. 3. Absorption curves of 1,6-diphenylhydrazodithiocarbamide derivatives in 1% aqueous alkali: 1) 1,6-diphenylhydrazodithiocarbamide; 2) 1-phenyl-6-(o-phenetyl)-hydrazodithiocarbamide; 3) 1-phenyl-6-(p-phenetyl)-hydrazodithiocarbamide.

carbazine was boiled for 1 hr under reflux in anhydrous alcohol with 2 g of p-phenetyl isothiocyanate. The yield of product was 3 g. The m.p. was 188° (from alcohol). The product was also obtained from 4-(p-phenetyl)-thiosemicarbazide and phenyl isothiocyanate. It also had m.p. 188° and did not depress the melting point of the product from 4-phenylthiosemicarbazide and p-phenetyl isothiocyanate.

1-Phenyl-6-(p-acetophenyl)-hydrazodithiocarbamide. The reaction was carried out with 2 g of 4-phenylthiosemicarbazide and 2.1 g of p-acetophenyl isothiocyanate. On recrystallization from alcohol, the product formed yellow platelets. The yield was 4.1 g.

1-Phenyl-6-(p-sulfamidophenyl)-hydrazodithiocarbamide was obtained from 2 g of 4-phenylthiosemicarbazide and 2.6 g of p-sulfamidophenyl isothiocyanate. The yield was quantitative.

1-(p-Phenetyl)-6-(p-sulfamidophenyl)-hydrazodithiocarbamide. The reaction was carried out with 2 g of 4-(p-phenetyl)-thiosemicarbazide and 2.0 g of p-sulfamidophenyl isothiocyanate. The yield was 3.6 g.

All the 1,6-diphenylhydrazodithiocarbamide derivatives given in Table 2 were obtained under conditions analogous to those described above.

SUMMARY

The synthesis of 18 substituted 4-phenylthiosemicarbazides and 39 unsymmetrical 1,6-diphenylhydrazodithiocarbamide derivatives, which have not been described in the literature, is described. The absorption spectra of the compounds synthesized were measured.

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CONJUGATED SYSTEMS

CXVII. DIRECTION OF ADDITION OF HALOGENS TO VINYLACETYLENES *

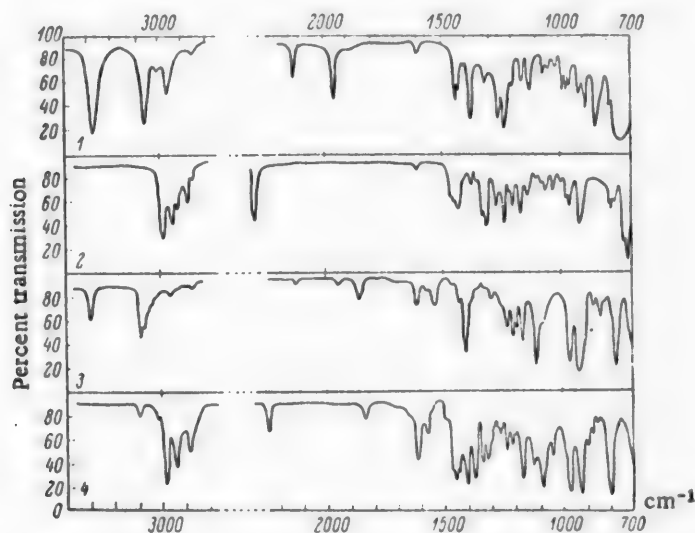
A. A. Petrov, Yu. I. Porfir'eva, and T. V. Yakovleva

Lensovet Leningrad Technological Institute

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A study of the reactions of vinylacetylenes with bromine and iodine chloride showed that, in both cases, the order of addition depended on the structure of the hydrocarbon [1-3]. Vinylacetylene and propenylacetylene gave predominantly allene dihalides (1,4 addition), while vinylalkylacetylenes, isopropenylacetylene, and unconjugated vinylacetylenes gave predominantly acetylene dihalides (3,4 addition). In contrast to bromine and iodine chloride, iodine added almost exclusively at the triple bond, regardless of the hydrocarbon structure [4].



Infrared transmission spectra. 1) Vinylacetylene dichlorides; 2) vinylethylacetylene dichlorides; 3) vinylacetylene bromoiodides; 4) vinylethylacetylene bromodiodides. Layer 32 μ .

* Enyne compounds. XL.

To complete the study of the order of addition of halogens to vinylacetylenes, it was necessary to establish the order of addition of chlorine and bromine iodide. Chlorine is interesting as an addend in that its adducts are usually incapable of rearranging under the reaction conditions (are further from the equilibrium state). With respect to activity, bromine iodide lies between bromine and iodine, and differs from them in showing polarity (dipole moment 0.4 D) [5].

We studied the chlorination of and the action of bromine iodide on two hydrocarbons which differ sharply in the order of addition of bromine and chlorine iodide, namely, vinylacetylene and vinyl ethylacetylene. The structure of the dihalides obtained was established by an investigation of their infrared spectra.

As was shown previously [6], the reaction of vinylacetylene with chlorine, even with high dilution, at low temperatures (down to -60°), and with a large excess of hydrocarbon, resulted in the predominant formation of tetrachlorides and other high-boiling products. Dichlorides could be isolated only in very small amounts.

A study of the infrared spectra of the dichlorides showed that they were a mixture of allene and acetylene adducts with a small amount of the 1,3-diene dichloride. The spectrum of the mixture of dichlorides investigated had intense bands characteristic of an allene grouping (1962 cm^{-1}), and a triple bond (2130 and 3300 cm^{-1}), and a very weak band corresponding to valence vibrations of a conjugated 1,3-diene grouping (1607 cm^{-1}). The bands in the region of $900\text{--}1000\text{ cm}^{-1}$, which could be assigned to deformation vibrations of a vinyl group, had a medium intensity (see figure, curve 1).

Thus, it was established that in the reaction with vinylacetylene, chlorine behaves analogously to bromine, with the only difference that chlorine forms a larger amount of the acetylene (3,4-addition) and a smaller amount of the 1,3-diene (1,2 addition) dichlorides. This characteristic is evidently connected with the lower tendency for isomerization at the moment of reaction of acetylene and allene dichlorides into 1,3-diene dichlorides as compared with the analogous dibromides.

However, it should be noted that these data on the order of addition of chlorine to vinylacetylene may be distorted due to differences in the rates of subsequent chlorination of the three possible dichlorides (which are actually formed).

A large amount of high-boiling products was also formed during the chlorination of vinyl ethylacetylene. Judging by the infrared spectrum, the dichloride was the acetylene compound with a very small amount of the 1,3-diene. The spectrum contained intense bands of the valence vibrations of a triple bond (2247 and 2256 cm^{-1}) and a very weak band of the valence vibrations of a double bond (1610 cm^{-1}) (see figure, curve 2).

Consequently, chlorine is analogous to bromine as regards the order of addition to vinyl ethylacetylene.

In contrast to chlorine, bromine iodide added to both hydrocarbons predominantly at the triple bond. A small amount of the acetylene dihalide was formed (addition at the double bond). The amount of allene adduct was insignificant.

The infrared spectra of the adducts showed clearly expressed bands characteristics of a 1,3-diene grouping substituted with halogen (1615 , 1540 , 966 , and 922 cm^{-1} in the case of vinylacetylene, and 1612 , 1570 , 966 , and 915 cm^{-1} in the case of vinyl ethylacetylene). Bands characteristic of an acetylene grouping (2124 cm^{-1} for vinylacetylene and 2246 cm^{-1} for vinyl ethylacetylene) were relatively weakly expressed. The frequency of the valence vibration of an allene system (1960 cm^{-1}) was not detected reliably (see figure, curves 3 and 4).

Thus, it was established that bromine iodide behaves similarly to iodine in addition reactions.

The difference in the order of addition of bromine and iodine to vinylacetylenes we previously explained by a difference in the addition mechanism, assuming that iodine reacts by a radical chain mechanism, while bromine adds according to an ionic scheme. It is possible that bromine iodide also adds by a radical mechanism, while chlorine adds by an ionic mechanism. In any case, the polarity of bromine iodide does not have an effect on the order of addition.

In all cases, we isolated the dihalides by vacuum distillation of the reaction products. To exclude possible errors due to isomerization of the reaction products during distillation, we also investigated the infrared spectra of the starting reaction mixtures. The various higher halides they contained made these spectra very complex, but they always contained frequencies belonging to those dihalides which we then isolated from these mixtures.

EXPERIMENTAL

Chlorination of vinylacetylene. To a solution of 52 g of vinylacetylene (threefold excess) in 50 ml of CCl_4 at -60° was added a solution of 23 g of chlorine in 150 ml of CCl_4 dropwise with vigorous stirring. Slight evolution of HCl was observed.

Distillation of the reaction mixture on a Widmer fractionating column at 50 mm yielded 3.6 g of a fraction of dichlorides. It had b.p. $65-67^\circ$ (50 mm), d^{20}_4 1.2289, n^{20}_D 1.5070. The residue weighed 23 g.

Found %: C 39.50, 39.38; H 3.28, 3.40; Cl 57.12, 57.66. $\text{C}_4\text{H}_4\text{Cl}_2$. Calculated %: C 39.06; H 3.27; Cl 57.66.

Infrared spectrum: 750 v.s., 790 av, 850 v.s., 896 s, 919 av, 962 av, 973 av, 986 av, 1016 w, 1047 w, 1070 w, 1130 av, 1160 av, 1204 w, 1243 v.s., 1262 s, 1318 s, 1377 s, 1403 v.w., 1428 w, 1442 av, 1607 w, 1962 s, 2130 av, 2860 w, 2969 av, 3005 w, 3060 s, 3280 v.s., cm^{-1} .

Chlorination of vinyl ethylacetylene. Under the conditions given above, 40 g of vinyl ethylacetylene (twofold excess) and 18 g of chlorine in CCl_4 (10% solution) yielded about 4 g of dichlorides with b.p. $77-78^\circ$ (20 mm), d^{20}_4 1.1317, n^{20}_D 1.4880 and 13.1 g of residue.

Found %: C 47.24, 47.74; H 5.21, 5.17; Cl 47.75, 46.90. $\text{C}_6\text{H}_8\text{Cl}_2$. Calculated %: C 47.71; H 5.34; Cl 46.96.

Infrared spectrum: 718 v.s., 732 s, 772 w, 785 w, 794 w, 920 s, 959 av, 972 av, 998 v.w., 1032 w, 1062 w, 1081 v.w., 1103 v.w., 1143 w, 1168 av, 1201 av, 1218 v.w., 1242 s, 1276 av, 1313 s, 1325 av, 1336 av, 1354 v.w., 1379 w, 1430 av, 1440 av, 1451 av, 1462 av, 1610 w, 2247 s, 2256 s, 2865 w, 2883 av, 2917 av, 2943 s, 2986 v.s., cm^{-1} .

Addition of bromine iodide to vinylacetylene. Bromine iodide was obtained by the usual method [7]. From 37 g (sevenfold excess) of vinylacetylene and 20.7 g of bromine iodide in 120 ml of ethyl chloride at -60° we obtained 21 g of bromoiodides. Distillation of them yielded a fraction (6.2 g) with b.p. $52-60^\circ$ (3 mm), d^{20}_4 2.2478 and n^{20}_D 1.6470. The residue weighed 12 g.

Found %: Br + I 80.75, 80.98; $\text{C}_4\text{H}_4\text{BrI}$. Calculated %: Br + I 79.89.

Infrared spectrum: 690 v.s., 772 v.s., 836 w, 864 w, 922 v.s., 966 v.s., 1080 av, 1109 v.s., 1172 s, 1195 av, 1208 av, 1292 v.w., 1407 s, 1429 w, 1540 av, 1566 v.w., 1615 av, 1850 w, 1946 v.w., 2124 v.w., 2966 v.w., 3017 v.w., 3038 v.w., 3065 av, 3087 w, 3296 av, cm^{-1} .

Addition of bromine iodide to vinyl ethylacetylene. From 16 g of vinyl ethylacetylene (twofold excess) in 60 ml of ethyl chloride and 20.7 g of bromine iodide in 60 ml of ethyl chloride we obtained 6.6 g of a fraction with b.p. $70-85^\circ$ (5 mm) and 16 g of residue. The bulk of the first fraction had the following constants: b.p. $73-75^\circ$ (4 mm), d^{20}_4 1.9093, n^{20}_D 1.5965.

Found %: Br + I 73.21, 72.99. $\text{C}_6\text{H}_8\text{BrI}$. Calculated %: Br + I 72.08.

Infrared spectrum: 685 v.s., 794 v.s., 852 v.w., 877 w, 888 w, 915 v.s., 966 v.s., 1038 av, 1088 v.s., 1121 av, 1169 s, 1207 av, 1233 av, 1259 w, 1274 v.w., 1316 av, 1335 av, 1372 av, 1399 s, 1434 av, 1454 av, 1460 av, 1570 av, 1612 s, 1840 w, 2246 av, 2876 av, 2936 s, 2976 v.s., 3015 v.w., 3094 w, cm^{-1} .

SUMMARY

1. The order of addition of chlorine and bromine iodide to vinylacetylene and vinyl ethylacetylene was studied.
2. It was established that chlorine adds to both hydrocarbons predominantly in the same way as bromine; the 1,4 adduct was mainly formed in the case of vinylacetylene and the 3,4 adduct (addition at the double bond), in the case of vinyl ethylacetylene.
3. It was shown that, as regards order of addition, bromine iodide is similar to iodine; addition occurs mainly at the triple bond, regardless of the structure of the starting hydrocarbon.

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CONJUGATED SYSTEMS

CXVIII. DIRECTION OF ADDITION OF BROMINE TO VINYLACETYLENE KETONES**

L. F. Chelpanova, V. D. Nemirovskii, A. A. Petrov,
and T. V. Yakovleva

Lensovet Leningrad Technological Institute

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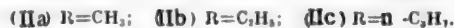
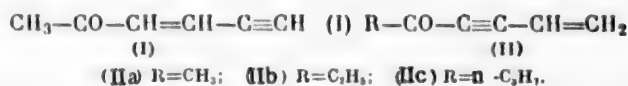
May, 1960

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In an investigation of the reactions of vinylacetylenes with electrophilic, nucleophilic, and radical reagents, rules for the order of addition were observed which are interesting in the theory of organic chemistry [1-4]. Thus, for example, the reactions of vinylacetylene and alkenylacetylenes with bromine gave predominantly allene dibromides (1,4 addition), while vinylalkylacetylenes added bromine to form acetylene dibromides (3,4 addition) [1,2].

It was interesting to compare these data with the results of experiments on the order of addition of bromine to vinylacetylene derivatives. Some work in this direction has already been carried out. For example, the addition of bromine to vinylacetylene alcohols [5] and methyl vinylacetylenecarboxylate [6] has been studied. In both cases, addition occurred predominantly at the double bond, i.e., the same rule was observed as for vinylalkylacetylenes.

In the present communication, we give the results of determining the order of addition of bromine to two types of vinylacetylene ketones (I) and (II).



We used infrared spectroscopy as a method of investigating the structure of the bromination products. It was previously shown that by this method it is easy to determine the order of addition of various addends to vinylacetylenes as it is a matter of choosing between three systems of multiple bonds, each of which has its own characteristic infrared frequencies [7].

The following comments may be made on the infrared spectra of the starting ketones. In the spectrum of ketone (I), the frequencies 2104 and 3284 cm^{-1} correspond to the acetylene grouping, the frequencies 1598 and

*Original Russian pagination. See C.B. Translation.

**Enyne compounds. XLI.

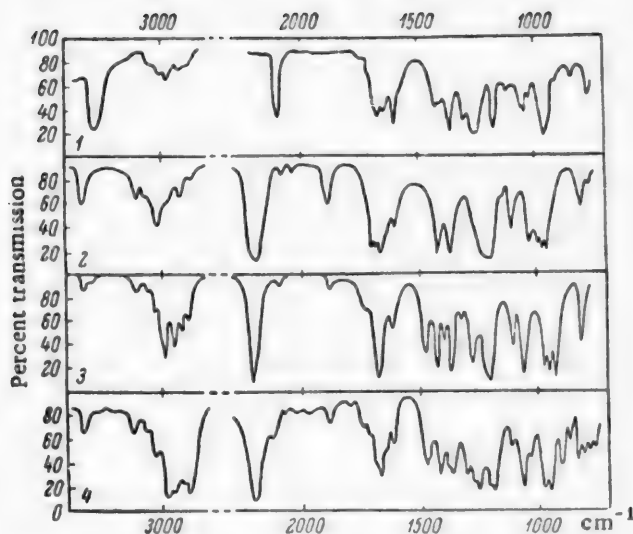


Fig. 1. Infrared transmission spectra: 1) hexen-3-yn-1-one-5; 2) hexen-1-yn-3-one-5; 3) hepten-1-yn-3-one-5; 4) octen-1-yn-3-one-5.

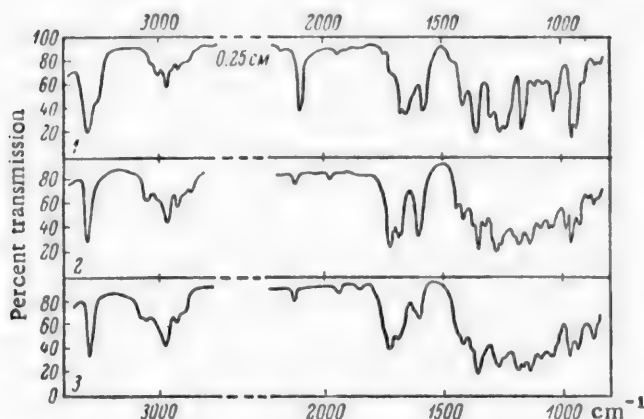


Fig. 2. Infrared transmission spectra of CCl_4 solutions: 1) hexen-2-yn-1-one-5 (I); 2) bromination products of ketone (I) with a 1:1 ratio; 3) bromination products of ketone (I) with a 1:1.5 ratio.

of bromine was used in the reaction, the triple bond did not disappear completely. Bromination in the 1,4 position, which is characteristic of enyne hydrocarbons with a terminal acetylene grouping, did not occur in the case of the ketones, as the spectra of the bromides did not show absorption characteristic of an allene grouping (1960 cm^{-1}) (Fig. 2).

The spectra of the bromination products of ketones of type (II) showed considerable weakening of the triple-bond frequency in comparison with the spectra of the starting ketones. The double-bond valence frequencies increased in intensity and new, lower frequencies appeared. The deformation frequencies of the vinyl group changed little. The absorption band of the carbonyl group spread toward higher frequencies. As in the first case, no frequencies of an allene system were detected here (Fig. 3).

960 cm^{-1} to the $-\text{CH}=\text{CH}-$ grouping, and $1668\text{--}1686 \text{ cm}^{-1}$ to the carbonyl group. In the spectra of ketones (IIa,b,c), the band of the valence vibrations of the triple bond (about 2195 cm^{-1}) has a higher intensity, and the band of the valence vibrations of the double bond (about 1600 cm^{-1}) has a lower intensity than in the spectrum of ketone (I). Intense bands of valence vibrations at about 970 and 940 cm^{-1} correspond to the vinyl group. In the spectra of all the ketones the frequencies of the multiple bonds are strongly reduced, due to conjugation. The band of the carbonyl group has a complex outline. The band in the region of 1170 cm^{-1} , characteristic of the group CH_3-CO , is differentiated only in the spectrum of ketone (I).

Intense absorption was observed in the region of $1220\text{--}1270 \text{ cm}^{-1}$. In the region of 3300 cm^{-1} there was a weak band, which may be an overtone [8]. Ketones with a terminal vinyl group (II) absorb at about 3100 cm^{-1} (Fig. 1).

To determine the order of addition of bromine to vinylacetylene ketones, we compared the infrared spectra of CCl_4 solutions of these ketones with the spectra of solutions of their bromination products in the same solvent. As the reaction mixture was not treated in any way to isolate the bromides, the data obtained undoubtedly refer to the initial bromination products.

A comparison of the spectra of solutions of ketone (I) and its bromination products (equimolar amount of bromine) showed that bromination led to considerable weakening of the frequencies associated with the acetylene bond and strengthening of absorption in the region of 1600 and 1720 cm^{-1} . These data indicate that the addition of bromine occurred predominantly at the triple bond. However, at the same time there was also bromination at the double bond with the formation of an unconjugated ketone (frequency 1720 cm^{-1}). The partial bromination of the double bond is also indicated by the fact that even when a 50% excess

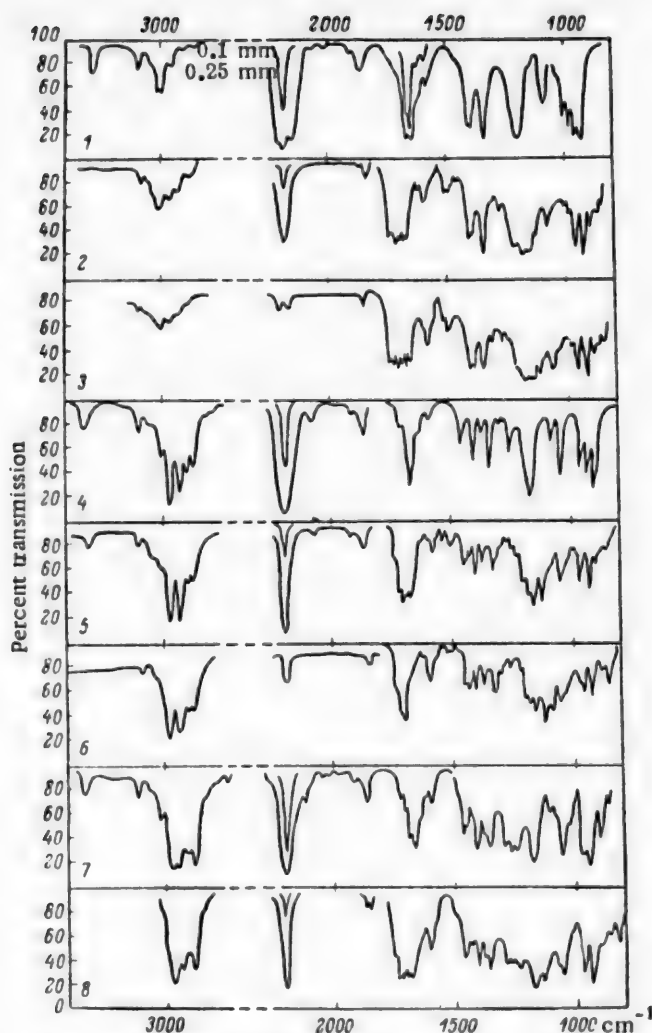


Fig. 3. Infrared transmission spectra of CCl_4 solutions: 1) hexen-1-yn-3-one-5 (IIa); 2) bromination products of ketone (IIa) with a ratio of 1:1; 3) bromination products of ketone (IIa) with a ratio of 1:1.5; 4) hepten-1-yn-3-one-5 (IIb); 5) bromination products of ketone (IIb) with a ratio of 1:1; 6) bromination products of ketone (IIb) with a ratio of 1:1.5; 7) octen-1-yn-3-one-5 (IIc); 8) bromination products of ketone (IIc) with a ratio of 1:1.

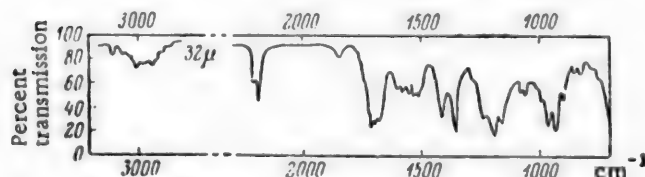


Fig. 4. Infrared transmission spectra of the dibromides of hexen-1-yn-3-one-5.

The data presented show that bromination of ketones of type (II) occurred at both multiple bonds; 1,4 addition was not observed.

We were unable to isolate dibromides of ketone (I); decomposition occurred during an attempt to distill them from the reaction mixture.

Dibromides of ketone (IIa) were isolated from the reaction mixture. An investigation of their infrared spectra showed that the correct conclusion was drawn in experiments with solutions: Ketone (IIa) added bromine to form acetylene and diene ketones. The spectrum contained frequencies of an acetylene group (2186 cm^{-1}) and a double bond ($1530\text{--}1606 \text{ cm}^{-1}$), and also the deformation frequencies of a vinyl group (932 and 967 cm^{-1}) (Fig. 4).

Thus, by the present investigation it was established that vinylacetylene ketones add bromine much less selectively than hydrocarbons of analogous structure. In this case, there is also complete absence of 1,4 addition. The comparatively high rate of bromine addition is noteworthy.

A triple bond normally shows low reactivity toward bromine. In our experiments the carbonyl group increased this reactivity. This effect is difficult to explain if bromination is regarded as electrophilic addition. It is most likely that nucleophilic addition of bromine occurs during the bromination of vinylacetylene ketones. In recent years analogous hypotheses have been put forward for the bromination of other organic compounds, including unsaturated ketones [9-11].

EXPERIMENTAL

Hexen-3-yn-1-one-5. Hexen-4-yn-1-ol-3 was prepared from crotonaldehyde and sodium acetylide in liquid ammonia [12]. The alcohol yield was 30% (on crotonaldehyde). Isomerization of this alcohol by sulfuric acid gave a 60% yield of hexen-3-yn-1-ol-5. Oxidation of the latter with chromic mixture gave hexen-3-yn-1-one-5 (15% yield).

B.p. $55\text{--}57^\circ$ (20 mm), d_4^{20} 0.9308, n_D^{20} 1.4951.

Infrared spectrum: 753 av. , 837 w. , 909 w. , 960 v.s. , 1018 av. , 1037 av. , 1052 av. , 1122 w. , 1176 v.s. , 1256 v.s. , 1297 s. , 1360 v.s. , 1424 av. , 1598 v.s. , 1645 s. , 1668 s. , 1686 s.

2104 s., 2893 v.w., 2927 w., 2977 av., 3011 w., 3042 v.w., 3284 v.s., cm^{-1} .

The 2,4-dinitrophenylhydrazone formed brown platelets (alcohol + dioxane) with m.p. 130° (decomp.) [12].

Hexen-1-yn-3-one-5 was prepared from magnesium vinylacetylide and acetic anhydride [13]. The yield was 30%.

B.p. $35-35.5^\circ$ (10 mm), d_4^{20} 0.9081, n_D^{20} 1.4840.

Infrared spectrum: 764 w., 797 av., 950 v.s., 972 v.s., 980 v.s., 1017 v.s., 1099 s., 1220 v.s., 1356 v.s., 1414 v.s., 1598 s., 1660 s., 1676 s., 1688 s., 1878 av., 2039 v.w., 2090 v.w., 2196 v.s., 2877 v.w., 2920 av., 2977 av., 3016 s., 3108 w., 3328 w., cm^{-1} .

2,4-Dinitrophenylhydrazone: m.p. 161° (alcohol + ethyl acetate).

Hepten-1-yn-3-one-5 was obtained analogously (from magnesium vinylacetylide and propionic anhydride) in 33% yield. The reaction product was stirred for a day with sodium carbonate solution for complete removal of the excess propionic anhydride.

B.p. $37-37.5^\circ$ (5 mm), d_4^{20} 0.8992, n_D^{20} 1.4843, MR 34.37; calc. 32.07.

Found %: C 77.77; H 7.52. $\text{C}_7\text{H}_8\text{O}$. Calculated %: C 77.77; H 7.41.

Infrared spectrum: 799 av., 913 v.s., 938 v.s., 963 v.s., 1051 v.s., 1091 av., 1188 v.s., 1265 s., 1310 w., 1352 v.s., 1383 av., 1414 v.s., 1464 s., 1604 av., 1672 v.s., 1883 w., 2088 v.w., 2196 v.s., 2878 av., 2909 av., 2943 s., 2983 s., 3022 av., 3055 v.w., 3108 w., 3335 v.w., cm^{-1} .

The 2,4-dinitrophenylhydrazone formed yellow needles with m.p. $133-134^\circ$ (alcohol).

Found %: N 19.69. $\text{C}_{13}\text{H}_{12}\text{O}_4\text{N}_4$. Calculated %: N 19.45.

Octen-1-yn-3-one-5 was obtained from magnesium vinylacetylide and butyric anhydride in 15% yield.

B.p. 41° (3 mm), d_4^{20} 0.8880, n_D^{20} 1.4823, MR 39.21; calc. 36.69.

Found %: C 78.15; H 8.19. $\text{C}_8\text{H}_{10}\text{O}$. Calculated %: C 78.65; H 8.21.

Infrared spectrum: 748 av., 770 av., 796 av., 815 av., 860 w., 889 s., 938 v.s., 966 v.s., 1019 av., 1054 v.s., 1106 w., 1179 v.s., 1244 v.s., 1268 v.s., 1292 s., 1356 s., 1379 s., 1408 s., 1463 av., 1602 av., 1663 v.s., 1692 s., 1708 w., 1725 w., 1875 w., 2061 v.w., 2123 v.w., 2193 v.s., 2740 v.w., 2881 v.s., 2907 v.s., 2939 v.s., 2967 v.s., 3020 av., 3107 w., 3328 w., cm^{-1} .

The 2,4-dinitrophenylhydrazone formed yellow needles with m.p. $73-74^\circ$ (alcohol).

Found %: N 18.55, 18.59. $\text{C}_{14}\text{H}_{14}\text{O}_4\text{N}_4$. Calculated %: N 18.54.

Bromination of ketones. To a solution of 0.01 mole of ketone in 5 ml of CCl_4 was added a solution of 0.011 or 0.015 mole of bromine in 4 ml of CCl_4 with vigorous stirring and cooling to -5 to 10° . The final solution was diluted to 10 ml. The spectrum of this solution was compared with that of a solution of 0.002 mole of ketone in 2 ml of CCl_4 .

The products from the bromination of 5.8 g of ketone (IIa) under the same conditions were vacuum distilled at 3 mm. This yielded 4.6 g of dibromides and 6.9 g of high-boiling products.

The dibromides had b.p. $85-105^\circ$ (4 mm), d_4^{20} 1.8081, n_D^{20} 1.5756.

Found %: Br 62.92, 62.12. $\text{C}_6\text{H}_6\text{OBr}_2$. Calculated %: Br 62.93.

In all cases, substitution was insignificant during bromination.

The infrared spectra were plotted with an IKS-14 spectrophotometer with LiF and NaCl prisms with a layer thickness of 0.1 and 0.25 mm for solutions and 0.032 mm for pure ketones.

SUMMARY

1. The order of addition of bromine to vinylacetylene ketones of the type $\text{R}-\text{CO}-\text{CH}=\text{CH}-\text{C}\equiv\text{CH}$ and $\text{R}-\text{CO}-\text{C}\equiv\text{C}-\text{CH}=\text{CH}_2$ was investigated.

2. It was shown that in both cases bromine addition occurred at both the triple and double bonds; 1,4 addition was not observed.

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REACTIONS OF CHLORINE-CONTAINING TELOMERS OF DIENES

III. PREPARATION OF ALDEHYDES AND KETONES FROM PRODUCTS OF ADDING TERT-BUTYL CHLORIDE TO BUTADIENE AND CHLOROPRENE

A. A. Petrov and Z. N. Kolyaskina

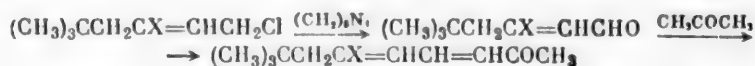
Lensovet Leningrad Technological Institute

Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 5, pp. 1450-1454,

May, 1960

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An investigation of the telomerization of dienes with saturated halogen derivatives showed that only tertiary alkyl halides give a good yield of monomeric adducts of the type $R-C_4H_6-Cl$ [1]. To determine the possibility of using this reaction in organic synthesis, we studied the conversions of the above halogen derivatives into unsaturated aldehydes and ketones with a tertiary carbon atom according to the following scheme.



The structure of the addition product of tert-butyl chloride and butadiene has been demonstrated previously by ozonization [1]. We investigated its infrared spectrum (Fig. 1, curve 1). This spectrum contained the frequencies 1669 and 971 cm^{-1} , which are characteristic of the grouping $-CH=CH-$, while the frequencies of valence and deformation vibrations of a vinyl group were absent. Thus, there was no doubt about the structure of the substance.

The adduct of tert-butyl chloride and chloroprene was obtained in our laboratory as early as 1953 [2]; however, no data on it were published in journals. As in the first case, the structure of the substance was previously

*Original Russian pagination. See C.B. translation.

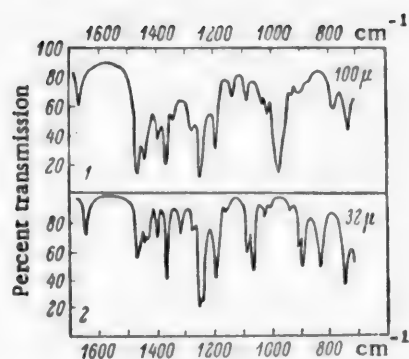


Fig. 1. Infrared transmission spectra:
1) 1-chloro-5,5-dimethylhexene-2;
2) 1,3-dichloro-5,5-dimethylhexene-2.

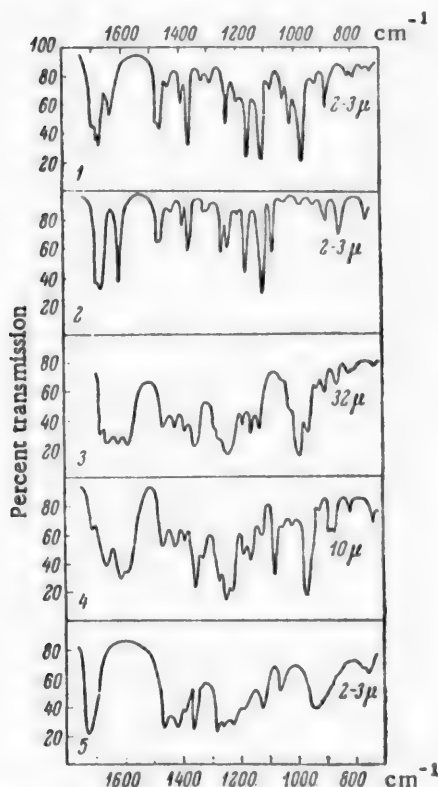


Fig. 2. Infrared transmission spectra:
1) 5,5-dimethylhexen-2-al; 2) 3-chloro-5,5-dimethylhexen-2-al; 3) 2,2-dimethylnonadien-4,6-one-8; 4) 4-chloro-2,2-dimethylnonadien-4,6-one-8; 5) 5,5-dimethylhexanal (with impurities).

demonstrated by ozonization. Its infrared spectrum (Fig. 1, curve 2) contained an intense band at the frequency of double-bond valence vibration (1645 cm^{-1}), which was narrower than in the previous case, and also the frequency of deformation vibrations of CH in the grouping $\text{CCl}=\text{CH}-$ (834 cm^{-1}). No bands which could be assigned to vibrations of a vinyl group were detected. Frequencies in the region of $1200\text{--}1250\text{ cm}^{-1}$ in both of the spectra investigated were ascribed to the presence of a tertiary grouping.

The chlorides were converted into the unsaturated aldehydes by means of the Sommelet reaction [3], which has already been used many times in our laboratory for the synthesis of terpene aldehydes [4].

From 1-chloro-5,5-dimethylhexene-2 we obtained 5,5-dimethylhexen-2-al (I), and from 1,3-dichloro-5,5-dimethylhexene-2, 3-chloro-5,5-dimethylhexen-2-al (II). Both aldehydes were colorless oils with the smell of hay. They became yellow during storage. They were insoluble in water, but dissolved readily in the usual organic solvents.

In the infrared spectrum of aldehyde (I) (Fig. 2, curve 1), three frequencies in the region of $1679\text{--}1702\text{ cm}^{-1}$ corresponded to the carbonyl group and the frequency of 1640 cm^{-1} , to the double bond. The deformation frequencies in the grouping $-\text{CH}=\text{CH}-$ corresponded to approximately the same frequency as in the starting chloride (977 cm^{-1}). The frequencies of 1114 and 1166 cm^{-1} were probably connected with the presence of the aldehyde group, and the frequencies of 1197 and 1234 cm^{-1} with the presence of the quaternary grouping.

The infrared spectrum of aldehyde (II) differed from that of aldehyde (I) (Fig. 2, curve 2) in a higher intensity, a displacement of the double-bond frequency into the long-wave region by 28 cm^{-1} , the absence of absorption in the region of $900\text{--}1000\text{ cm}^{-1}$, and the presence of a quite intense band at 840 cm^{-1} (deformation vibration of CH in the grouping $-\text{CCl}=\text{CH}-$).

Both aldehydes reacted readily with hydrazine derivatives; under normal conditions they yielded readily crystallizable semicarbazones and 2,4-dinitrophenylhydrazones.

Condensation of the aldehydes with acetone yielded diene ketones as slightly yellowish oils with a pleasant smell. In the infrared spectra of these ketones, the frequencies of 1594 and 1627 cm^{-1} and 1594 and 1615 cm^{-1} , respectively, corresponded to the double bond and the frequencies of 1666 and 1663 cm^{-1} , respectively, to the carbonyl group. The intense bands in the region of $970\text{--}990\text{ cm}^{-1}$ could be ascribed to deformation vibrations in the grouping $-\text{CH}=\text{CH}-$ (Fig. 2, curves 3 and 4).

As a result of the addition of the first mole of hydrogen, hydrogenation of aldehyde (I) over colloidal palladium yielded predominantly 5,5-dimethylhexenal (Fig. 2, curve 5); however, the substance contained an alcohol (established by the infrared spectrum). Consequently, the hydrogenation under these conditions was not completely selective.

The investigation presented showed that by means of telomerization it is possible to obtain from dienes a series of unsaturated aldehydes and ketones with quaternary carbon atoms.

EXPERIMENTAL

Preparation of 5,5-dimethylhexen-2-al. The starting 1-chloro-5,5-dimethylhexene-2 was obtained by addition of tert-butyl chloride (0.25 mole) to butadiene (0.3 mole) in the presence of 1 g of anhydrous zinc chloride and 0.1 g of hydroquinone. The reaction mixture was shaken mechanically in a closed, thick-walled bottle for 40 hr. Then 4 ml of diethylamine was added. The precipitate was removed by filtration. The liquid was vacuum distilled. This yielded 11 g (25%) of 1-chloro-5,5-dimethylhexene-2 with b.p. 47-48° (10 mm).

Infrared spectrum: * 735 s., 787 av., 873 w., 900 w., 932 w., 971 v.s., 1012 w., 1031 w., 1085 av., 1138 w., 1199 av., 1245 v.s., 1276 w., 1342 v.w., 1368 s., 1387 av., 1441 s., 1473 s., 1669 av., cm^{-1} .

A mixture of 27 g of 1-chloro-5,5-dimethylhexene-2, 31 g of urotropine (20% excess), and 200 ml of dichloroethane was shaken in a closed, thick-walled bottle for 80 hr. To the crystalline mass obtained was added 150 ml of water, whereupon the reaction mixture separated into two layers. The dichloroethane layer was washed twice with water. Distillation of this layer yielded 8 g of unreacted starting chloride.

The aqueous layer (combined with wash waters from the dichloroethane layer) was carefully separated from insoluble materials, 160 ml of 30% formalin solution added, and the mixture steam distilled with the solution gradually added to the distillation flask as distillate was removed. The distillate (1.5-2 liters) was saturated with sodium chloride and extracted 3-4 times with ether. The ether extracts were dried with baked sodium sulfate, the ether removed on a water bath, and the residue (19 g) vacuum distilled (3 mm). This yielded the following fractions: 1st up to 39°, 0.5 g; 2nd, 39-39.5°, 14.9 g (64% yield); residue 1.3 g.

5,5-Dimethylhexen-2-al: b.p. 55-55.5° (10 mm), d_{20}^{20} 0.8357, n_D^{20} 1.4490, MR 40.50, calc. 38.69.

Found %: C 76.40, 76.08; H 11.23, 11.05. M 130.2, 123.7. $\text{C}_8\text{H}_{14}\text{O}$. Calculated %: C 76.14; H 11.18, M 126.2.

Infrared spectrum: * 735 w., 797 w., 813 w., 889 av., 933 av., 977 v.s., 1011 s., 1032 av., 1076 w., 1114 v.s., 1166 s., 1197 w., 1234 s., 1290 w., 1322 w., 1369 s., 1392 av., 1433 w., 1468 s., 1473 s., 1640 s., 1679 s., 1690 s., 1702 s., 2705 s., 2739 s., 2816 s., 2869 v.s., 2911 v.s., 2946 v.s., cm^{-1} .

Semicarbazone: m.p. 181-181.5° (aqueous alcohol). It formed fine, colorless platelets.

Found %: N 22.75, 23.18. $\text{C}_9\text{H}_{17}\text{ON}_3$. Calculated %: N 22.93.

2,4-Dinitrophenylhydrazone: M.p. 188-188.2° (alcohol). It formed orange platelets.

Found %: N 18.21, 18.43. $\text{C}_{14}\text{H}_{18}\text{O}_4\text{N}_4$. Calculated %: N 18.30.

Preparation of 2,2-dimethylnonadien-4,6-one-8. Into a flask with a mechanical stirrer, dropping funnel, and thermometer were placed 10 g of 5,5-dimethylhexen-2al and 42 g (tenfold excess) of anhydrous acetone. The mixture was cooled to -10 to -12° and stirred vigorously while a solution of sodium alcoholate (0.8 g of sodium in 17.5 ml of alcohol) was added dropwise. The reaction mixture thereupon acquired an orange-red color. After the mixture had been stirred for 5 min, 2.6 g of tartaric acid and 18 ml of water were added, and the acetone was then steam distilled (until the appearance of turbid drops in the receiver). After cooling, the oily layer was separated from the aqueous one, dried with baked sodium sulfate, and vacuum distilled (10 mm). The following fractions were obtained: 1st up to 70°, 2.4 g; 2nd, 70-105°, 1 g; 3rd, 105-115°, 7.6 g (57% yield); 4th, 115 to 140°, 0.9 g; residue 0.9 g.

Redistillation of the third fraction yielded 2,2-dimethylnonadien-4,6-one-8.

B.p. 108-110° (10 mm), d_{20}^{20} 0.8721, n_D^{20} 1.5000, MR 56.07, calc. 52.08.

* Layer thickness 0.1 mm, instrument - IKS-2.

** Layer thickness 2-3 μ .

Found %: C 78.39, 78.88; H 11.09, 11.09. M 162.8, 159.1. $C_{11}H_{18}O$. Calculated %: C 79.46; H 10.91; M 166.4.

Infrared spectrum: * 733 w., 803 w., 817 w., 863 w., 896 av., 932 w., 960 s., 993 v.s., 1133 s., 1160 s., 1194 s., 1234 v.s., 1358 v.s., 1393 s., 1428 s., 1464 s., 1594 s., 1627 s., 1662 s., 1689 s., cm^{-1} .

Semicarbazone: m.p. 154-154.5° (from aqueous alcohol). It formed fine, colorless crystals.

Found %: N 18.64, 18.92. $C_{12}H_{21}ON_3$. Calculated %: N 18.82.

2,4-Dinitrophenylhydrazone: m.p. 178.5-179° (alcohol). It formed fine, orange-red crystals.

Found %: C 58.93, 59.14; H 6.55, 6.60; N 16.36, 16.37. $C_{17}H_{22}O_4N_4$. Calculated %: C 58.94; H 6.40; N 16.18.

Preparation of 3-chloro-5,5-dimethylhexen-2-al. By shaking a mixture of 23 g of tert-butyl chloride (0.25 mole) and 26.6 g of freshly distilled chloroprene (0.3 mole) in the presence of 1 g of zinc chloride and 0.1 g of hydroquinone for 40 hr we obtained 25.5 g (47.0%) of 1,3-dichloro-5,5-dimethylhexene-2.

B.p. 73° (10 mm), d^{20}_4 1.0313, n^{20}_D 1.4698.

Infrared spectrum: * * 745 s., 834 s., 897 s., 906 av., 933 w., 1099 w., 1026 w., 1072 s., 1093 s., 1153 w., 1193 s., 1237 v.s., 1246 v.s., 1276 w., 1314 av., 1368 s., 1398 av., 1433 av., 1442 av., 1468 s., 1645 av., cm^{-1} .

A mixture of 32 g of 1,3-dichloro-5,5-dimethylhexene-2, 30 g of urotropine (20% excess) and 300 ml of dichloroethane was shaken for 80 hr. The solid reaction mass was treated in the same way as in the previous experiment. This yielded 14.5 g of aldehyde (51%). About 7 g of dichloride was recovered.

3-Chloro-5,5-dimethylhexen-2-al: b.p. 76-77° (10 mm), d^{20}_4 0.9963, n^{20}_D 1.4760, MR 45.48; calc. 43.56.

Found %: C 60.04, 59.71; H 8.33, 8.25; Cl 22.15, 22.31; M 160.1, 164.3. $C_9H_{15}OCl$. Calculated %: C 59.81; H 8.16; Cl 22.07. M 160.6.

Infrared spectrum: * * * 748 av., 841 av., 889 av., 930 w., 973 w., 1050 w., 1077 s., 1110 v.s., 1168 s., 1198 w., 1232 s., 1250 s., 1300 w., 1313 w., 1371 s., 1392 av., 1434 w., 1470 s., 1612 v.s., 1676 v.s., cm^{-1} .

Semicarbazone: m.p. 195-195.5° (alcohol). It formed colorless needles.

Found %: N 19.72, 19.79. $C_9H_{16}ON_3Cl$. Calculated %: N 19.35.

2,4-Dinitrophenylhydrazone: m.p. 148.5-149.5° (alcohol). It formed orange needles.

Found %: N 17.16, 16.99. $C_{14}H_{17}O_4N_4Cl$. Calculated %: N 16.44.

Preparation of 4-chloro-2,2-dimethylnonadien-4,6-one-8. Under the conditions described for the preparation of 2,2-dimethylnonadien-4,6-one-8, 7 g of 3-chloro-5,5-dimethylhexen-2-al and 34 ml of anhydrous acetone yielded 4 g (40%) of crude condensation product with b.p. 114-122° (3 mm). Redistillation gave quite pure 4-chloro-2,2-dimethylnonadien-4,6-one-8 as a liquid with a pleasant fruity odor, which was insoluble in water.

B.p. 122-129° (8 mm), d^{20}_4 0.9930, n^{20}_D 1.5175. MR 61.20; calc. 56.94.

Found %: C 65.31, 65.76; H 8.88, 9.16; Cl 17.13, 17.48. $C_{11}H_{17}OCl$. Calculated %: C 65.82; H 8.54; Cl 17.66.

Infrared spectrum: 746 av., 817 av., 888 av., 897 av., 934 w., 972 v.s., 1023 w., 1065 w., 1087 s., 1139 av., 1166 av., 1197 av., 1237 s., 1256 s., 1278 s., 1334 av., 1360 s., 1396 av., 1428 av., 1472 av., 1594 s., 1615 s., 1663 s., 1690 w., 1712 av., cm^{-1} .

The semicarbazone formed fine, slightly yellowish crystals with m.p. 177-177.5°.

Found %: C 56.46, 56.63; H 8.17, 8.18; N 16.09, 16.16; Cl 14.87, 14.91. $C_{12}H_{20}ON_3Cl$. Calculated %: C 55.91; H 7.82; N 16.32; Cl 13.75.

* Layer thickness 0.01 mm.

** Layer thickness 0.032 mm.

*** Layer thickness 2-3 μ .

The 2,4-dinitrophenylhydrazone formed fine red crystals with m.p. 172.5-173°.

Found %: N 14.59, 14.88. $C_{17}H_{21}O_4N_4Cl$. Calculated %: N 14.71.

The infrared spectra were plotted on an IKS-14 spectrophotometer (with the exception of the case mentioned) with an NaCl prism.

SUMMARY

1. By means of the Sommelet reaction, the adducts of tert-butyl chloride with butadiene and chloroprene were converted into two aldehydes with quaternary carbon atoms, namely 5,5-dimethylhexen-2-al and 3-chloro-5,5-dimethylhexen-2-al.

2. Some reactions of these aldehydes were investigated, namely those with hydrazine derivatives (semi-carbazones and 2,4-dinitrophenylhydrazones were prepared), and with acetone in the presence of sodium alcoholate (2,2-dimethylnonadien-4,6-one-8 and 4-chloro-2,2-dimethylnonadien-4,6-one-8 were prepared).

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INVESTIGATION OF ISOQUINOLINE COMPOUNDS

XVII. SYNTHESIS OF 4',5'-DIMETHOXY-7-(1"-METHYL-6",7"-DIMETHOXYTETRAHYDRO-ISOQUINOLYL)-3,4,5,6,7,8-HEXAHYDROBENZ-(1,2:1',2')-QUINOLIZINE, C-NOREMETINE

R. P. Evstigneeva, N. K. Gavrina, and N. A. Preobrazhenskii

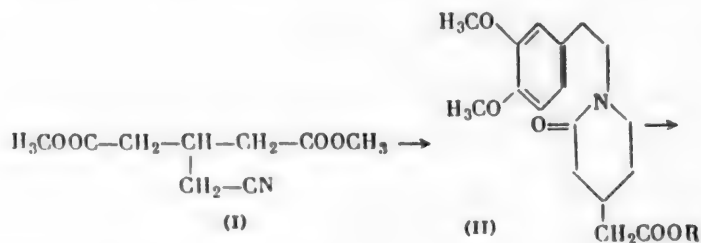
Moscow Institute of Fine Chemical Technology

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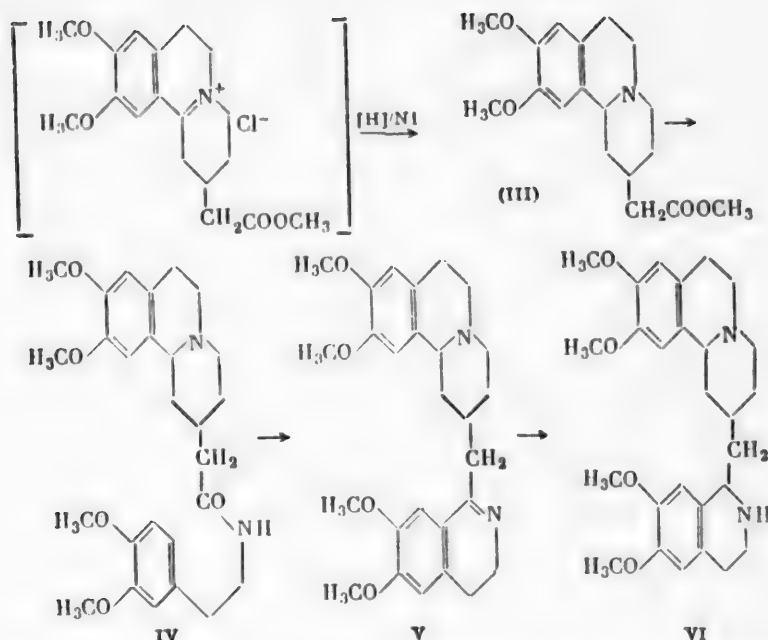
May, 1960

Original article submitted June 2, 1959

C-Noremetine differs from the alkaloid emetine in lacking an ethyl group at C₆. Several methods of preparing this compound have been described in the literature [1-4]. We undertook a synthesis of C-noremetine (VI) according to a scheme developed for emetine in order to compare the final bases and intermediate compounds obtained by the different routes, which is necessary to solve some problems on the stereoisomerism of the natural alkaloid.



*Original Russian pagination. See C.B. translation.



The methyl ester of β -cyanomethylglutaric acid (I) was obtained by selective hydrolysis and decarboxylation of the methyl ester of β -(cyano, carboethoxy)-methylglutaric acid — an intermediate compound in the synthesis of the alkaloid emetine [5]. Reductive condensation of (I) with homoveratrylamine yielded the methyl ester of N-[β -(3,4-dimethoxyphenyl)-ethyl]- α -piperidone- γ -acetic acid (II, R = CH₃). Hydrolysis of the latter in acid and alkaline media gave good yields of the corresponding acid (II, R = H). Cyclization of compound II (R = CH₃) with phosphorus oxychloride and subsequent hydrogenation of the quaternary chloride in the presence of Raney nickel yielded the methyl ester of 4',5'-dimethoxy-3,4,5,6,7,8-hexahydrobenz-(1,2;1',2')-quinolizyl-7-acetic acid (III). The reaction of ester (III) with homoveratrylamine yielded the amide (IV), which gave dehydronoremetine (V) on cyclization with phosphorous oxychloride. Reduction of (V) in the presence of Raney nickel yielded C-noremetine (VI).

EXPERIMENTAL

Methyl ester of β -cyanomethylglutaric acid (I). To a solution of sodium methylate from 3.4 g of sodium and 50 ml of anhydrous methanol were added 2.66 ml of water and 40 g of the methyl ester of β -(cyano, carboethoxy)-methylglutaric acid. The mixture was left for 12 hr and then heated for 1 hr on a boiling water bath. The excess alcohol was removed in vacuum. To the residue was added 40 ml of water. The unhydrolyzed tricarboxylic ester was extracted with ether (2 \times 50 ml). The aqueous solution was acidified with hydrochloric acid (to Congo). The oil liberated was extracted with ether (2 \times 50 ml) and the extract dried with sodium sulfate. The ether was removed and the residue heated at 180° for 30 min. To the cooled residue was added 75 ml of benzene and the solution washed with 5% alkali (3 \times 10 ml). After removal of the solvent, the residue was distilled. The yield was 13.55 g (46%, without allowance for the unhydrolyzed tricarboxylic ester).

B.p. 137.5–138° (2.5 mm), d_4^{20} 1.1404, n_D^{20} 1.4502. MR_D 46.68; calc. 46.89.

Found %: C 54.62, 54.40; H 6.76, 6.66; N 6.92, 6.88. C₉H₁₃O₄N. Calculated %: C 54.27; H 6.57; N 7.03.

Methyl ester of N-[β -(3,4-dimethoxyphenyl)-ethyl]- α -piperidone- γ -acetic acid (II, R = CH₃). A mixture of 12 g of the methyl ester of β -cyano-methylglutaric acid and 45 g of homoveratrylamine in 60 ml of anhydrous methanol was hydrogenated in the presence of 3 g of Raney nickel at 110 atm and 110–115° for 2 hr. The catalyst was removed and the alcohol evaporated in vacuum. The residue was dissolved in benzene and washed with 3% hydrochloric acid and then an aqueous solution of sodium bicarbonate. The solvent was removed and the residue vacuum distilled. The yield was 4 g (20.2%). The b.p. was 200–202° (0.2 mm). After some time the piperidone crystallized. It separated from ether as colorless crystals, which were readily soluble in alcohol and benzene, but insoluble in water. The m.p. was 56.5–58°.

Found %: C 64.16; H 7.72, 7.41; N 4.40, 4.13. $C_{18}H_{25}O_5N$. Calculated %: C 64.46; H 7.51; N 4.17.

N-[β -(3,4-Dimethoxyphenyl)-ethyl]- α -piperidone- γ -acetic acid (II, R - H). a) To the sodium methylate prepared from 0.11 g of sodium and 20 ml of anhydrous methanol was added 1.6 g of the piperidone in 6 ml of methanol and 0.1 g of water. On the following day the reaction mixture was heated on a boiling water bath for 1 hr. The alcohol was removed in vacuum and the residue dissolved in water. The aqueous solution was shaken with ether to remove the unhydrolyzed piperidoneacetic ester, neutralized with hydrochloric acid, and extracted with chloroform. The solvent was removed. The residue was a colorless crystalline substance with m.p. 147-147.5°. After recrystallization from a benzene-ether mixture (2:1), the acid was isolated as right trihedral prisms. The yield was 1.3 g (85%). The m.p. was 148-148.5°.

b) A mixture of 0.7 g of the methyl ester of N-[β -(3,4-dimethoxyphenyl)-ethyl]- α -piperidone- γ -acetic acid and 8 ml of 6% hydrochloric acid was boiled gently for 1 hr. The solvent was removed in vacuum. Benzene was added to the residue and removed in vacuum several times. The acid was recrystallized from a mixture of benzene and ether. The yield was 0.5 g (83.5%).

M.p. 148-148.5°

Found %: C 63.27, 63.53; H 7.05, 7.37; N 4.41, 4.31. $C_{17}H_{23}O_5N$. Calculated %: C 63.53; H 7.21; N 4.35.

Methyl ester of 4',5'-dimethoxy-3,4,5,6,7,8-hexahydrobenz-(1,2:1',2')-quinolizyl-7-acetic acid (III). Under the conditions described previously [5], 5.2 g of the methyl ester of N-[β -(3,4-dimethoxyphenyl)-ethyl]- α -piperidone- γ -acetic acid was cyclized with phosphorus oxychloride and the chloride of the quaternary base then hydrogenated in the presence of Raney nickel to yield the base as a colorless crystalline material. The yield was 3.6 g (65.9%). The m.p. was 75.6-76° (ether).

Found %: C 67.78, 67.81; H 7.91, 7.73; N 4.59, 4.65. $C_{18}H_{25}O_4N$. Calculated %: C 67.72; H 7.84; N 4.38.

The hydrochloride was a colorless, crystalline substance, which was readily soluble in water, less so in alcohol, and insoluble in ether. The m.p. was 192.5-193.5°.

Found %: C 60.95, 61.15; H 7.18, 7.31; N 4.01, 4.20. $C_{18}H_{26}O_4NCl$. Calculated %: C 60.92; H 7.36; N 3.93.

β -(3'',4''-Dimethoxyphenyl)-ethylamido-4',5'-dimethoxy-3,4,5,6,7,8-hexahydrobenz-(1,2:1',2')-quinolizyl-7-acetic acid (IV). A mixture of 1.3 g of the methyl ester of 4',5'-dimethoxy-3,4,5,6,7,8-hexahydrobenz-(1,2:1',2')-quinolizyl-7-acetic acid and 2.2 g of β -(3,4-dimethoxyphenyl)-ethylamine was heated at 180-190° in a stream of nitrogen for 4 hr. The cooled reaction mass was triturated with dry ether. The amide was isolated as a colorless, crystalline substance, which was readily soluble in alcohol and benzene, less soluble in acetone, and difficultly soluble in water and ether. It was recrystallized from acetone. The yield was 1.68 g (94%). The m.p. was 149-150°.

Found %: C 69.35, 69.25; H 7.7, 7.8; N 5.75, 5.70. $C_{27}H_{36}O_5N_2$. Calculated %: C 69.23; H 7.69; N 5.98.

4',5'-Dimethoxy-7-(1''-methyl-6'',7''-dimethoxy-3'',4''-dihydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenz-(1,2:1',2')-quinolizine (V). A solution of 0.82 g of β -(3'',4''-dimethoxyphenyl)-ethylamido-4',5'-dimethoxy-3,4,5,6,7,8-hexahydrobenz-(1,2:1',2')-quinolizyl-7-acetic acid in 5 ml of chloroform was heated with 4 ml of phosphorus oxychloride for 4 hr. The usual treatment yielded the dehydro base as a colorless, amorphous substance. The yield was 0.6 g (75.1%). The m.p. was 63-64°.

Found %: C 72.40, 72.06; H 7.57, 7.60; N 6.21. $C_{27}H_{34}O_4N_2$. Calculated %: C 71.97; H 7.60; N 6.21.

The oxalate was isolated as a colorless, crystalline substance, which was readily soluble in water, less so in alcohol, and insoluble in ether. The m.p. was 185-186.5° (alcohol).

Found %: C 59.2; H 6.03; N 4.10. $C_{31}H_{38}O_{18}N_2$. Calculated %: C 59.03; H 6.07; N 4.44.

4',5'-Dimethoxy-7-(1''-methyl-6'',7''-dimethoxytetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenz-(1,2:1',2')-quinolizine, C-noremefine. A 3.46-g sample of dehydro-C-noremefine was dissolved in anhydrous methanol and hydrogenated in an autoclave in the presence of Raney nickel at an initial pressure of 90 atm and at 55° for 2 hr. The catalyst was removed and the alcohol evaporated in vacuum. The base of noremefine was isolated as a colorless, amorphous substance. The yield was 2.8 g (80.6%). The base was converted to the oxalate.

The oxalate was recrystallized from alcohol and the base again liberated. The colorless amorphous substance was readily soluble in organic solvents and insoluble in water. The m.p. was 53-54.5°.

Found %: C 71.74; H 8.26; N 5.92. $C_{27}H_{36}O_4N_2$. Calculated %: C 71.79; H 8.00; N 6.17.

The oxalate had m.p. 167.5-168.5° (from alcohol).

Found %: C 58.73; H 6.41; N 4.36. $C_{27}H_{36}O_4N_2 \cdot 2C_2H_2O_4$. Calculated %: C 58.87; H 6.33; N 4.43.

The hydrochloride had m.p. 201-202.5° (from alcohol with ether).

Found %: N 5.23; Cl 13.41; $C_{27}H_{36}O_4N_2 \cdot 2HCl$. Calculated %: N 5.33; Cl 13.52.

SUMMARY

C-Noremefine was synthesized.

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SYNTHETIC INVESTIGATIONS AMONG ISOMERIC COCAINES

V. SYNTHESIS OF METHYL ESTERS OF TROPAN-3 α -OL-2 β -CARBOXYLIC ACID, ALLOECGONINE, AND TROPAN-3 α -OL-2 α -CARBOXYLIC ACID, ALLOPSEUDOECGONINE

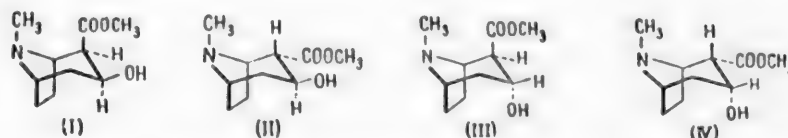
G. I. Bazilevskaya, M. S. Bainova, K. M. Dyumaev, and
N. A. Preobrazhenskii

Moscow Institute of Fine Chemical Technology

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The methyl esters of tropan-3-ol-2-carboxylic acids may exist as four racemic and eight optically active isomeric forms (I-IV and the corresponding antipodes and racemates).



Cocaine and pseudococaine, corresponding to conformations (I) and (II), are encountered in natural sources, while the alloalkaloids (III and IV) are not found in plants.

* Original Russian pagination. See C.B. translation.

Methyl esters of tropan-3-ol-3-carboxylic acids may be obtained by reduction of the methyl ester of tropan-3-one-2-carboxylic acid, when the formation of one or another isomer depends both on the hydrogenation conditions and on the nature of the reducing agent.

From the "third ecgonine" of Willstätter [2], Zeile and Schultz [1] obtained the methyl ester of alloecgonine (rac. III, m.p. 203-205° for polyhydrate). The method of isolating the "third ecgonine" was not described in this work, which makes it difficult to repeat it. Findlay [3] reported the reduction of the methyl ester of tropan-3-one-2-carboxylic acid, in the presence of platinum oxide, to the methyl ester of alloecgonine (rac. III, m.p. 81.5-83.5°) and alkaline hydrolysis of this gave allo- and allopseudoecgonines, which were then esterified to the methyl esters of alloecgonine (rac. III, picrate m.p. 204°) and allopseudoecgonine (rac. IV, m.p. 80°; picrate m.p. 136°). However, even in the next paper, Findlay [4] described the methyl ester of (+)-alloecgonine as a liquid, without giving physicochemical constants.

To prepare isomeric ecgonines, we studied a series of catalytic, electrochemical, and chemical hydrogenation methods.

When Raney nickel was used as the catalyst for reduction of the methyl ester of tropan-3-one-2-carboxylic acid, we obtained an oily substance which according to analyses and molecular refraction corresponded to the methyl ester of ecgonine, but whose constants differed considerably from those of the latter.

The wide boiling range of the substance obtained, and also the fact that its iodomethylate deformed at 224.5°, i.e., considerably below the melting point (298-299.5°), compelled us to assume that the substance obtained was a mixture of isomers. According to Auwers's rule [5], the low refractive index (1.4814) and specific gravity (1.0972) in comparison with those of the methyl ester of ecgonine (d_4^{20} 1.1469, n_D^{20} 1.4880), indicates that in the mixture formed the isomer with a 2,3-trans structure predominated. The methyl ester of pseudoecgonine (rac. II) is known to be insoluble in ether [6]. The fact that the substance obtained was readily soluble in ether indicated that the reduction of the methyl ester of tropan-3-one-2-carboxylic acid in the presence of Raney nickel formed mainly the methyl ester of alloecgonine (rac. III) with some methyl ester of allopseudoecgonine (rac. IV). The amount of the latter in the mixture increased with more drastic hydrogenation conditions.

Fractional distillation of the mixture of ecgonine methyl esters obtained and fractional crystallization of the picrates yielded two individual methyl esters, which should be considered as the methyl ester of alloecgonine (rac. III) and the methyl ester of allopseudoecgonine (rac. IV). Thus, in the given case of hydrogenation in the presence of Raney nickel, as in the case of the reduction of tropinone [7] and N-methyl-3-carbomethoxy-4-piperidone [8], 3-axial alcohols are formed.

EXPERIMENTAL

1. Methyl esters of allo- and allopseudotropan-3-ol-2-carboxylic acids (rac. III and IV). a) A solution of 20 g of the methyl ester of tropan-3-one-2-carboxylic acid in 360 ml of absolute methanol was hydrogenated in the presence of Raney nickel at 15-20° and atmospheric pressure with mechanical stirring. When 2.25 liters of hydrogen had been absorbed over a period of 45-50 hr and no color was produced with ferric chloride, the catalyst was removed and washed with 65 ml of absolute methanol. After removal of the solvent, the residue was distilled. A colorless, oily substance was obtained. The yield was 12.4 g (62%).

B.p. 87-102° (0.35 mm), d_4^{20} 1.0972, n_D^{20} 1.4814, M_R 51.71, calc. 51.10.

Found %: C 59.80, 60.10; H 8.61, 8.45; N 7.08, 7.09. $C_{10}H_{17}O_3N$. Calculated %: C 60.28, H 8.59; N 7.02.

b) Into a stainless steel, rotating autoclave were placed 20 g of the methyl ester of tropan-3-one-2-carboxylic acid in 360 ml of absolute methanol and 10 g of Raney nickel. Reduction was carried out at an initial pressure of 100 atm and 15-20° for 3-4 hr. The subsequent treatment of the reaction mixture and isolation of the substance produced were as in the previous experiment.

B.p. 90-91° (0.2 mm), d_4^{20} 1.1151, n_D^{20} 1.4862, M_R 51.32; calc. 51.10.

Found %: C 60.70, 60.50; H 8.34, 8.54; N 7.37, 7.33. $C_{10}H_{17}O_3N$. Calculated %: C 60.28; H 8.59; N 7.02.

Picrates of methyl esters of allo- and allopseudotropin-3-ol-2-carboxylic acids. a) To a solution of 1.7 g of the methyl esters of allo- and allopseudoecgonines (experiment a) in 7 ml of absolute methanol was added 1.85 g of picric acid in 20 ml of absolute methanol. The picrate deposited was separated and washed with absolute methanol (1 ml) and ether (6 ml). The yield of crude picrate was 2.4 g (65.7%). M.p. 155-165° (deformed at 122°). The filtrate was concentrated to one-third of the initial volume. A further 0.2 g of picrate was isolated. The m.p. was 116-130° (deformed at 114°). Repeated recrystallization from absolute methanol yielded the picrates of allopseudoecgonine and alloecgonine.

Picrate of the methyl ester of allopseudotropin-3-ol-2-carboxylic acid, allopseudoecgonine. The yield was 0.65 g (17.8%). The m.p. was 196-198° (deformed at 195°).

Found %: C 44.80; H 4.40; N 12.76. $C_{16}H_{20}O_{10}N_4$. Calculated %: C 44.87; H 4.71; N 13.08.

The melting point was depressed by admixture with picrates of methyl esters of isomeric ecgonines.

Picrate of methyl ester of allotropin-3-ol-2-carboxylic acid, alloecgonine. The yield was 0.72 g (19.7%). The m.p. was 126-131° (deformed at 125°).

Found %: C 44.34; H 4.82; N 12.88. $C_{16}H_{20}O_{10}N_4$. Calculated %: C 44.87; H 4.71; N 13.08.

A mixture of the picrate of the methyl ester of alloecgonine with the picrate of the methyl ester of allopseudoecgonine melted at 125-140° (deformed at 122°).

b) To a solution of 1.2 g of the methyl esters of allo- and allopseudoecgonines obtained in experiment 1b in 20 ml of absolute methanol was added 1.32 g of picric acid in 14 ml of absolute methanol. The yield of picrate was 1.4 g (54.3%). The m.p. was 189-191° (deformed at 187°). Concentration of the filtrate to 2.5 ml yielded a further 0.8 g (31.0%) of picrate. The m.p. was 116-120° (deformed at 115°).

I. Recrystallization of the 1.4 g of crude picrate from 84 ml of absolute methanol yielded the picrate of the methyl ester of allopseudoecgonine. The yield was 1.1 g (42.6%). The m.p. was 199-201° (deformed at 196°).

Found %: C 44.57; H 4.87; N 13.32. $C_{16}H_{20}O_{10}N_4$. Calculated %: C 44.87; H 4.71; N 13.08.

II. Recrystallization of the 0.8 g of picrate from 5.6 ml of absolute methanol yielded the picrate of the methyl ester of alloecgonine. The yield was 0.3 g (11.6%). The m.p. was 125-130° (deformed at 124°).

Found %: N 13.28. $C_{16}H_{20}O_{10}N_4$. Calculated %: N 13.08.

Hydrochloride of the methyl ester of alloecgonine. A sample (0.55 g) of the picrate of the methyl ester of alloecgonine with m.p. 126-131° (deformed at 125°) was dissolved at 0 to +2° in 5 ml of dilute (4:1) hydrochloric acid. The picric acid was extracted with benzene (4 x 15 ml). The aqueous solution was neutralized with potassium carbonate at 0 to +2° and the base extracted with chloroform (60 ml) and dried with sodium sulfate. Removal of the chloroform yielded an oily substance. The yield was 0.17 g (66.5%). A solution of 0.17 g of the base (methyl ester of alloecgonine) in 1 ml of absolute methanol was neutralized with an ether solution of hydrogen chloride at 0°. The hydrochloride of the methyl ester of alloecgonine was obtained as a light yellow, thick oil. The yield was 0.16 g (79.6%).

Found %: N 5.89; Cl 14.92. $C_{10}H_{17}O_3N \cdot HCl$. Calculated %: N 5.94; Cl 15.05.

Hydrochloride of the methyl ester of allopseudoecgonine. A 0.56-g sample of the picrate of the methyl ester of allopseudoecgonine with m.p. 196-199° (deformed at 195°) was dissolved with cooling (0 to +2°) in 5 ml of dilute (4:1) hydrochloric acid. The rest of the process was as described for the isomeric methyl ester of alloecgonine. Removal of the chloroform yielded an oily substance. The yield was 0.13 g (49.9%). A solution of 0.13 g of the methyl ester of allopseudoecgonine in 1 ml of absolute methanol was neutralized with an ether solution of hydrogen chloride with cooling (0°). The yield was 0.12 g (78%). The m.p. was 188-189.5° (decomp.; deformed at 186°) (from absolute isopropyl alcohol).

Found %: C 51.30; H 7.63; N 5.82; Cl 14.4. $C_{10}H_{17}O_3N \cdot HCl$. Calculated %: C 50.95; H 7.69; N 5.94; Cl 15.05.

The melting point of a mixture of the hydrochlorides of the methyl esters of the isomeric ecgonines was depressed.

SUMMARY

1. The hydrogenation of the methyl ester of tropan-3-one-2-carboxylic acid to the methyl esters of isomeric tropan-3-ol-2-carboxylic acids in the presence of Raney nickel was studied.

2. It was shown that this reduction is stereodirected and gives 3-hydroxy axial isomers: the methyl ester of alloecgonine and the methyl ester of allopseudoecgonine.

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TERTIARY TRIHYDRIC ACETYLENIC ALCOHOLS AND THEIR CONVERSIONS

XX. STRUCTURE OF THE DEHYDRATION PRODUCTS OF ETHYLENIC 1,2,5-TRIOLS

V. I. Nikitin and G. I. Likhtenshtein

Institute of Chemistry, Academy of Sciences of the Tadzhik SSR

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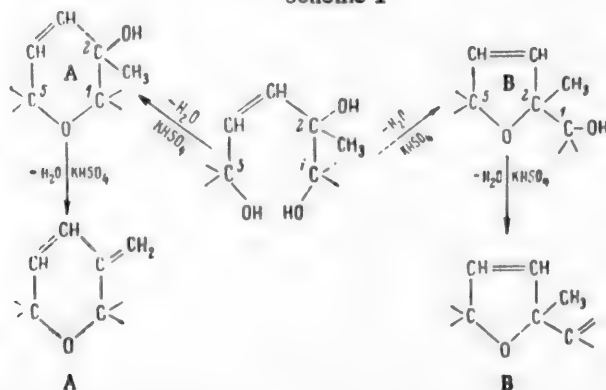
May, 1960

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An investigation which was published previously by one of us and Timofeeva [1], and which concerned the dehydration of ethylenic 1,2,5-triols with dilute sulfuric acid showed that under these conditions a triol molecule loses one molecule of water at the expense of two hydroxyl groups. The residue of the triol molecule is cyclized through the oxygen atom to an unsaturated heterocyclic alcohol.

In this work it was reported that the dehydration products could have either a dihydropyran (A) or a dihydrofuran structure (B) (scheme 1).

Scheme 1



*Original Russian pagination. See C.B. translation.

Attempts to use oxidation with potassium permanganate to demonstrate which of these two structures should be assigned to the products obtained did not give unequivocal results, though they indicated that the dihydropyran structure (A) was more probable.

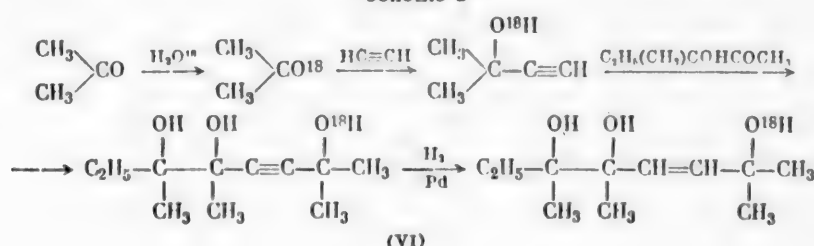
The present work was undertaken to demonstrate the structure of these products unequivocally. For solving this problem we decided to use labeled oxygen O^{18} . On being mixed with heavy water, compounds with a carbonyl oxygen exchange their oxygen comparatively readily for the oxygen of the heavy water [2]. By making use of this we obtained the ketones with O^{18} we required, and used them for the synthesis of acetylenic glycerols by the method developed by one of us [3,4]. Depending on whether the condensation was carried out with the carbonyl oxygen of the hydroxy ketone, or the hydroxyl oxygen of the labeled acetylenic carbinol, the final triols contained labeled oxygen in position 2 or 5. Subsequent hydrogenation of these glycerols [5] yielded the required ethylenic 1,2,5-triols with labeled oxygens.

The ethylenic triols thus synthesized were dehydrated with potassium bisulfate. The triol molecule first yielded one molecule of water and then a second. In each case, the water liberated was collected separately, and the isotopic composition determined. This made it possible to determine accurately the hydroxyl groups through which the triol was dehydrated, and thus establish unequivocally the structure of its dehydration products. However, we first had to study the dehydration of triols with potassium bisulfate, the use of which made it possible to collect the water thus liberated; sulfuric acid, which was used previously as the dehydrating agent, was unsuitable in this case.

The data obtained are given in Table 1. They show that the dehydration of ethylenic triols with potassium bisulfate proceeds in the same direction as with sulfuric acid. The reaction here is somewhat complicated by the secondary dehydration, so that it formed not only the product from the elimination of one water molecule from the triol (high-boiling fraction), but also the product of further dehydration of the high-boiling fraction to give a low-boiling fraction. The high-boiling fraction could be separated readily from the low-boiling one by vacuum distillation, and subsequent dehydration of it with potassium bisulfate made it possible to determine the position of the hydroxyl remaining in the molecule after the first dehydration (see scheme 1).

Table 1 shows that when the dehydration was carried out at no higher than 130° , even with 1.5 moles of potassium bisulfate per mole of triol dehydrated, there was almost always much more of the high-boiling product than of the low-boiling one.

Scheme 2



Analogously, from $\begin{array}{c} \text{OH} \\ | \\ \text{C}_2\text{H}_5-\text{C}-\text{CO}^{18} \\ | \quad | \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$
we obtained 3,4,7-trimethyloct-5-ene-3,7-diol-4-ol- O^{18}

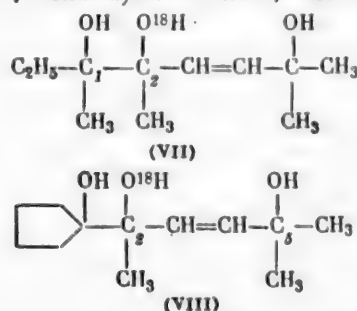


TABLE 1

Results of Dehydrating Ethylenic 1,2,5-Triols by Vacuum Distillation over Potassium Bisulfate

Structural formula, name, and number of ethylenic triol dehydrated	Amt. of potassium bisulfate used in moles per mole of triol dehydrated (in g)	Bath temperature	Dehydration product yield (in % on triol dehydrated)	
			high-boiling fraction - boiling point (pressure in mm)	low-boiling fraction - boiling point (pressure in mm)
$ \begin{array}{c} \text{OH} \quad \text{OH} \quad \quad \text{OH} \\ \quad \quad \quad \\ \text{CH}_3 - \text{C} - \text{C} - \text{CH} = \text{CH} - \text{C} - \text{C}_2\text{H}_5 \\ \quad \quad \quad \\ \text{CH}_3 \quad \text{CH}_3 \quad \quad \text{CH}_3 \end{array} $ (I) 2,3,6-Trimethyloct-4-ene-2,3,6-triol	1.0	110—120°	70—72° (8) 48.0	52—54° (8) 26.55
The same (I)	0.6	130	72—74° (8) 82	—
$ \begin{array}{c} \text{OH} \quad \text{OH} \quad \quad \text{OH} \\ \quad \quad \quad \\ \text{C}_2\text{H}_5 - \text{C} - \text{C} - \text{CH} = \text{CH} - \text{C} - \text{C}_2\text{H}_5 \\ \quad \quad \quad \\ \text{CH}_3 \quad \text{CH}_3 \quad \quad \text{CH}_3 \end{array} $ (II) 3,4,7-Trimethylnon-5-ene-3,4,7-triol	1.0	90	89—91° (8) 25.5	66—68° (8) 38
$ \begin{array}{c} \text{OH} \quad \text{OH} \quad \quad \text{OH} \\ \quad \quad \quad \\ \text{C}_6\text{H}_{11} - \text{C} - \text{C} - \text{CH} = \text{CH} - \text{C} - \text{C}_6\text{H}_{11} \\ \quad \quad \quad \\ \text{CH}_3 \quad \quad \quad \text{CH}_3 \end{array} $ (III) 2,4-Di-(1-hydroxycyclohexyl)-but-3-en-2-ol	1.0	120	120—122° (2) 40	112—114° (2) 35
$ \begin{array}{c} \text{OH} \quad \text{OH} \quad \quad \text{OH} \\ \quad \quad \quad \\ \text{C}_6\text{H}_{11} - \text{C} - \text{C} - \text{CH} = \text{CH} - \text{C} - \text{CH}_3 \\ \quad \quad \quad \\ \text{CH}_3 \quad \quad \quad \text{CH}_3 \end{array} $ (IV) 5-Methyl-2-(1-hydroxycyclohexyl)-hex-3-ene-2,5-diol	1.5	130	107—108° (8) 55	84—85° (8) 16
$ \begin{array}{c} \text{OH} \quad \text{OH} \quad \quad \text{OH} \\ \quad \quad \quad \\ \text{C}_5\text{H}_9 - \text{C} - \text{C} - \text{CH} = \text{CH} - \text{C} - \text{CH}_3 \\ \quad \quad \quad \\ \text{CH}_3 \quad \quad \quad \text{CH}_3 \end{array} $ (V) 5-Methyl-2-(1-hydroxycyclopentyl)-hex-3-ene-2,5-diol	1.0	120	99—108° (8) Not de- termined	73—74° (7.5) Not de- termined

TABLE 2

Results of Determination of O^{18} Content of Water from Various Sources

Expt. No.	Water examined and its source	Sample (in g)		$\frac{CO_2^{16}}{CO_2^{18}} \cdot \frac{100}{2}$	$\frac{O^{18}}{O^{16}} \cdot 100$ in water examined	Enrichment of water examined relative to natural water
		water	potassium carbonate			
1	Water containing 6.1% of H_2O^{18}	0.050	0.048	4.4	5.96	29.8
2	Distilled natural water containing 0.29% H_2O^{18}	0.050	0.042	0.2	0.20	1.0
3	Water isolated during dehydration of 3,4,7-trimethyloct-5-ene-3,4-diol-7-ol- O^{18} (VI)	0.045	0.048	0.41	0.56	2.8
4	Water isolated during dehydration of high-boiling fraction (b.p., 73-75° at 8 mm) obtained by dehydration of triol (VI)	0.045	0.045	0.2	0.20	1.0
5	Water isolated during dehydration of 5-methyl-2-(hydroxycyclopentyl)-hex-3-en-2-ol- O^{18} -5-ol (VIII)	0.050	0.031	0.40	0.50	2.5
6	Water isolated during dehydration of high-boiling fraction (b.p., 90-100° at 8 mm) obtained by dehydration of triol (VIII)	0.045	0.049	1.1	1.50	7.5
7	Water isolated during dehydration of 3,4,7-trimethyloct-5-en-4-ol- O^{18} -3,5-diol (VII)	0.050	0.048	0.23	0.24	1.2

By scheme 2 we synthesized two triols containing O^{18} : 3,4,7-trimethyloct-5-ene-3,4-diol-7-ol- O^{18} (VI) and 5-methyl-2-(1-hydroxycyclopentyl)-hex-3-en-2-ol- O^{18} -5-ol (VIII).

Triols (VI), (VII), and (VIII) containing labeled oxygen were dehydrated, and the water thus liberated collected and assayed for isotopic composition on a mass spectrograph. The assay results are given in Table 2. In the first two experiments of this table, we give data on the analysis of water with a known H_2O^{18} content, which indicate the reliability of the method. In experiment 3 we give the results of analyzing the water liberated during the dehydration of triol (VI). The water was found to be enriched by a factor of 2.8 in heavy oxygen as compared with natural water. This indicates that during the dehydration of triol (VI), the hydroxyl was eliminated from position 5, and that it was removed during the liberation of the first molecule of water from the triol dehydrated, as further dehydration of the high-boiling fraction gave water that was quite unenriched in heavy oxygen in comparison with natural water, as experiment 4 shows.

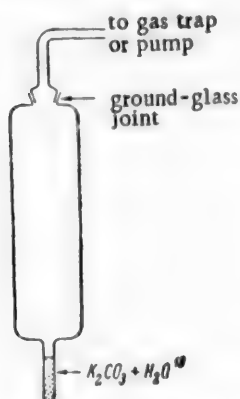
If triol (VII) (Table 2, experiment 7) or triol (VIII) (experiment 5), i.e., triols containing O^{18} in the hydroxyl in position 2, was hydrogenated, then the first molecule of water liberated was either almost unenriched in heavy oxygen (as in experiment 7) or, if it was enriched (as in experiment 5, by a factor of 2.5 in comparison with natural water), then this enrichment was due to the fact that, simultaneous with the dehydration of the triol, there was also partial dehydration of the high-boiling fraction. When this high-boiling fraction was dehydrated separately (Table 2, experiment 6), it gave water which was enriched in heavy oxygen by a factor of 7.5 as compared with natural water.

Thus, the hydroxyl in position 2 did not participate in the formation of the first molecule of water which was eliminated from the ethylenic triol dehydrated, resulting in cyclization of the molecule; the hydroxyl in this position passed completely into the high-boiling fraction. Dehydration of the triol occurred at the expense of the hydroxyls in positions 1 and 5. Consequently, the dehydration products of the triols investigated were substituted dihydropyrans, which confirms the previous hypothesis [1] that the dehydration occurs in such a way that the eliminated water molecule is derived from hydroxyl 5 and hydroxyl hydrogen 1 of positions 1 and 5, respectively.

As we showed in the present work, the substituted dihydropyransols may be dehydrated to unsaturated heterocyclic compounds with two double bonds, one of which is in the nucleus and the other is semicyclic (see scheme 1). However, there is the possibility that the latter may migrate into the nucleus to give a substituted pyran and, therefore, we can say nothing definite as yet on the structure of the dehydration products of the substituted dihydropyransols.

EXPERIMENTAL

Analysis of water for O^{18} . As water cannot be analyzed directly on a mass spectrograph [2], it was necessary to transfer the oxygen from the water to CO_2 . None of the procedures described in the literature were suitable for our case. The point was that we had a small amount of water (0.1-0.2 g), which also contained organic impurities, introduced as a result of the dehydration. A micromethod based on isotopic equilibration of the water sample with K_2CO_3 was therefore developed.* This method prevented the introduction of impurities into the mass spectrograph. The procedure was as follows: The sample of water examined, in which was dissolved a definite amount of potassium carbonate, was placed in a small vessel (15-20 ml in volume) with a finger 3 mm in diameter and 20 mm long at the bottom (see figure). The finger was heated on a boiling water bath for 20 min. The following exchange reaction occurred in the solution:



Rapid evaporation was prevented by closing the finger with a cork. When isotopic equilibrium had been established in the mixture, the cork was removed, pieces of pumice and earthenware were placed in the finger, and the water evaporated by heating. The potassium carbonate remaining in the finger was heated in vacuum for 15 min to remove ether and other volatile organic impurities. Then concentrated sulfuric acid was poured into the vessel, which was connected to a previously evacuated gas trap. On shaking, the sulfuric acid percolated into the finger and decomposed the potassium carbonate according to the reaction



The carbon dioxide liberated was frozen out in the gas trap with liquid nitrogen, and the air entering from the vessel was pumped off. The carbon dioxide thus collected was assayed for isotopic composition on an MS-1 mass spectrograph, which showed the percentage ratio O^{18}/O^{16} , with an accuracy of up to 0.1%.**

The O^{18} content of the water examined was calculated by the equation

$$g = g^1 \left(0.99 + \frac{m}{n} \right) - 0.2 \frac{m}{n}, \quad (1)$$

where g^1 is the percent O^{18} content of the carbon dioxide, g is the percent O^{18} content of the water, and m and n are the relative numbers of oxygen atoms participating in the exchange in carbonate and water, respectively.

Preliminary Study of Dehydration of Acetylenic 1,2,5-Triols by Potassium Bisulfate

1. Dehydration of 2,3,6-trimethyloct-4-ene-2,3,6-triol (I) (see Table 1). A mixture of 5.5 g of 2,3,6-trimethyloct-4-ene-2,3,6-triol (b.p. 117-118° at 2 mm), 3.4 g of potassium bisulfate, and traces of hydroquinone was placed in a Favorskii flask, which was heated to 110-120° on a bath of Wood's alloy. The dehydration products distilled at 8 mm. These were dried with Na_2SO_4 and distilled. Two fractions were collected: 1st, b.p. 52-54° (8 mm), 1.2 g; and 2nd, b.p. 70-72° (8 mm), 2.4 g. The first fraction was apparently 2,6,6-trimethyl-2-ethyl-5-methylenedihydropyran, the product of further dehydration of the second fraction.

* The method presented below was developed by G. I. Likhtenshtein.

** The mass spectrographic determinations were carried out in the Institute of Chemical Physics, Academy of Sciences, USSR, by V. I. Gorshkov.

Investigation of 1st fraction.

B.p. 52-54° (8 mm), d_4^{20} 0.8717, n_D^{20} 1.4508, M_R 51.24; calc. 51.50.

Found %: C 79.56, 79.35; H 10.60, 10.70. $C_{11}H_{18}O$. Calculated %: C 79.51; H 10.38.

No hydroxyl group was present. The reaction for a carbonyl group with 2,4,-dinitrophenylhydrazine hydrochloride was negative.

A solution of 0.221 g of the substance in 18 ml of acetic acid was hydrogenated over platinum oxide (Adams catalyst) for 2 hr. It absorbed 74 ml of hydrogen (calculated for 2 moles - 72 ml).

The second fraction (2.4 g) with b.p. 70-72° (8 mm), n_D^{20} 1.4555 corresponded to 2,5,6,6-tetramethyl-2-ethylidihydropyran-5-ol, described by one of us and Timofeeva [1].

2. Dehydration of 18 g of the same triol (I) at 130° with 7 g of $KHSO_4$ gave one fraction (13.5 g) with b.p. 72-74° (8 mm), n_D^{20} 1.4556, which was found to be the 2,5,6,6-tetramethyl-2-ethylidihydropyran-5-ol mentioned above.

3. Dehydration of 2,5,6,6-tetramethyl-2-ethylidihydropyran-5-ol (b.p. 72-74° at 8 mm and n_D^{20} 1.4556) with 7.5 g of $KHSO_4$ at 170° gave a product which almost completely corresponded to the first fraction with b.p. 52-54° (8 mm), n_D^{20} 1.4508 obtained in experiment 1.

4. Dehydration of 3,4,7-trimethylnon-5-ene-3,4,7-triol (II). A mixture of 12 g of (II) (b.p. 126-128° at 2 mm) with 7 g of $KHSO_4$ was heated to 90°. After the water had been removed, two fractions were collected: 1st, b.p. 66-68° (6 mm), 3.8 g; and 2nd, b.p. 89-91° (8 mm), 2.8 g. The first fraction was evidently 2,6-dimethyl-2,6-diethyl-5-methylenedihydropyran, the dehydration product of the second fraction.

Investigation of 1st fraction.

B.p. 66-68° (6 mm), d_4^{20} 0.8729, n_D^{20} 1.4556, M_R 56.63; calc. 56.12.

Found %: C 79.58, 79.92; H 11.36, 11.34. $C_{12}H_{20}O$. Calculated %: C 80.00; H 11.11.

Reactions for hydroxyl and carbonyl groups were negative.

In the hydrogenation of 0.2420 g of this fraction in 18 ml of acetic acid over platinum oxide (Adams catalyst), 77 ml of hydrogen was absorbed in 2 hr (calculated for 2 mole of hydrogen - 71 ml).

The second fraction (2.8 g) with b.p. 89-91° (8.5 mm), n_D^{20} 1.4598 corresponded to 5-methyl-2,6-dispirocyclohexanedihydropyran-5-ol [1].

5. Dehydration of 2,4-di-(1-hydroxycyclohexyl)-but-3-en-2-ol (III). A mixture of 13.5 g of substance (m.p. 110-112°) and 7.5 g of $KHSO_4$ with traces of hydroquinone was heated to 120°. After removal of the water from the mixture of dehydration products, two fractions were collected.

The first fraction (4 g) was evidently 2,6-dispirocyclohexane-5-methylenedihydropyran.

B.p. 112-114° (2 mm), d_4^{20} 0.9766, n_D^{20} 1.5076, M_R 70.75; calc. 70.20.

Found %: C 82.21, 82.08; H 10.31, 10.42. $C_{16}H_{24}O$. Calculated %: C 82.75; H 10.35.

A solution of 0.349 g of this substance in 18 ml of acetic acid was hydrogenated over platinum oxide (Adams catalyst) for 2 hr. It absorbed 84 ml of hydrogen (calculated for 2 moles of hydrogen - 78 ml).

The second fraction (5 g) with b.p. 120-122° (2 mm), n_D^{20} 1.5078 corresponded to 5-methyl-2,6-dispirocyclohexanedihydropyran-5-ol [1].

6. Dehydration of cis-5-methyl-2-(1-hydroxycyclohexyl)-hex-3-ene-2,5-diol (IV). A mixture of 18.5 g of the substance (m.p. 101-103°) and 15 g of $KHSO_4$ with traces of hydroquinone was heated to 130°. Two fractions were isolated.

The first fraction (8.5 g) was evidently 2,2-dimethyl-5-methylene-6-spirocyclohexanedihydropyran.

B.p. 84-85° (8 mm), d_4^{20} 0.934, n_D^{20} 1.4804, M_R 58.66; calc. 58.54.

Found %: C 81.12, 80.92; H 10.61, 10.38. $C_{13}H_{20}O$. Calculated %: C 81.25; H 10.51.

Reactions for hydroxyl and carbonyl groups were negative.

In the hydrogenation of 0.3030 g of this fraction in 12 ml of anhydrous methanol over platinum oxide, 44 ml of hydrogen was absorbed in 2 hr (calculated for 1 mole of hydrogen - 41.5 ml).

When 0.3105 g of the substance in 15 ml of acetic acid was hydrogenated over platinum oxide for 1 hr, 105 ml of hydrogen was absorbed (calculated for 2 moles of hydrogen - 97 ml).

The second fraction (2.7 g) with b.p. 107-108° (8 mm), n_D^{20} 1.4825 corresponded to 2,2,5-trimethyl-6-spirocyclohexanedihydropyran-5-ol [1].

7. Dehydration of 5-methyl-2-(1-hydroxycyclopentyl)-hex-3-ene-2,5-diol (V). A mixture of 18 g of substance (m.p. 129-130°) and 10 g of $KHSO_4$ with traces of hydroquinone was heated to 120°. Two fractions were isolated: 1st, b.p. 73-74° (7.5 mm), which was evidently 2,2-dimethyl-5-methylene-6-spirocyclopentane-dihydropyran; and 2nd, b.p. 99-100° (8 mm).

Investigation of 1st fraction.

B.p. 73-74° (7.5 mm), d_4^{20} 0.9299, n_D^{20} 1.4795, M_R 54.30; calc. 53.99.

Found %: C 80.58, 80.73; H 10.10, 10.02. $C_{12}H_{18}O$. Calculated %: C 80.89; H 10.11.

Reactions for carbonyl and hydroxyl groups were negative.

In the hydrogenation of 0.330 g of this substance in 18 ml of acetic acid over platinum oxide, 105 ml of hydrogen was absorbed in 36 min (calculated for 2 moles - 86 ml).

The second fraction, with b.p. 99-100° (8 mm), n_D^{20} 1.4826, corresponded to 2,2,5-trimethyl-6-spirocyclopentanedihydropyran-5-ol [1].

3,4,7-Trimethyloct-5-ene-3,4,-diol-7-ol- O^{18} (VI)

Preparation of acetone containing O^{18} . A mixture of 21 g of anhydrous acetone and 6 g of H_2O containing 6.1% of O^{18} with a small amount of sulfuric acid was kept at 20° for 850 hr. The mixture was then distilled, and the acetone fraction dried with calcium chloride and redistilled. To the labeled product obtained was added 28 g of anhydrous acetone. The acetone prepared in this way was used to synthesize 3,4,7-trimethyloct-5-ene-3,4-diol-7-ol- O^{18} with b.p. 117-119°. Hydrogenation of this triol over palladium on chalk yielded 3,4,7-trimethyloct-5-ene-3,4-diol-7-ol- O^{18} (VI) [4,5].

Dehydration of 3,4,7-trimethyloct-5-ene-3,4-diol-7-ol- O^{18} . A mixture of 19 g of 3,4,7-trimethyloct-5-ene-3,4-diol-7-ol- O^{18} and 6.5 g of potassium bisulfate with traces of hydroquinone was heated until rapid evolution of water from the reaction mixture began (130°). The water was collected, washed several times with ether, and sealed in an ampoule for mass spectrographic analysis.

In 0.045 g of this water was dissolved 0.048 g of potassium carbonate. The latter, after isotopic exchange, was treated as described to give a mixture of $C^{18}O_2$ and $C^{16}O_2$, which was analyzed on a mass spectrograph and shown to contain 0.41% of O^{18} . The O^{18} content of the water was calculated (Table 2, experiment 3).

If, in Eq. (1), \underline{m} is replaced by the weight of potassium carbonate \underline{b} , divided by its molecular weight, and \underline{n} is replaced by the weight of water \underline{a} divided by the molecular weight of water, Eq. (1) assumes the following form:

$$g = g' \left(0.99 + 39 \frac{b}{a} \right) - 0.08 \frac{b}{a}, \quad (2)$$

where g' is the percent O^{18} content of the CO_2 and g is the percent O^{18} content of H_2O .

The O^{18} content of the water examined in the given experiment (experiment 3), calculated by this formula, was found to equal 0.56%.

The dehydration products were vacuum distilled to give two fractions: 1st, b.p. 52-54° (8 mm), n_D^{20} 1.4505, 3 g, which was the product of the elimination of two water molecules; 2nd, with b.p. 73-75° (8 mm), n_D^{20} 1.4556, 13 g, which was the product of the elimination of one water molecule from the original triol.

Dehydration of the second fraction with b.p. 73-75° (8 mm). A mixture of 13 g of the substance and 7 g of potassium bisulfate with traces of hydroquinone was heated to 170-180°. At this temperature the reaction products distilled together with the water, forming an emulsion. The latter was centrifuged and the aqueous layer separated, washed with ether, and distilled. The purified water was sealed in an ampoule for analysis for O^{18} .

In 0.045 g of this water was dissolved 0.045 g of potassium carbonate. The O^{18} content of the CO_2 liberated from the potassium carbonate, which was determined with a mass spectrograph, was 0.2%, and the O^{18} content of the water, calculated from Eq. (2), was 0.2%. Thus, the high-boiling fraction, which was the product from the elimination of one water molecule from the triol, lacked a hydroxyl containing O^{18} .

The layer of reaction products was diluted with ether, dried with potassium carbonate, and distilled. It was largely a fraction with b.p. 52-54° (8 mm), n_D^{20} 1.4505.

3,4,7-Trimethyloct-5-ene-3,7-diol-4-ol- O^{18} (VII)

Methylethylacetyl- O^{18} -carbinol was prepared by treating methylethylacetylcarbinol (b.p. 148-150°, n_D^{20} 1.4220) with 4.5 g of water containing 6.1% of O^{18} and a small amount of sulfuric acid. The mixture was shaken at 20° for 150 hr. The water was then removed by distillation, and the methylethylacetylcarbinol dried over baked Na_2SO_4 and distilled. We collected a fraction with b.p. 147-149°, n_D^{20} 1.4222. To the product obtained was added 15 g of unlabeled methylethylacetylcarbinol.

3,4,7-Trimethyloct-5-yne-3,7-diol-4-ol- O^{18} was synthesized according to the same scheme as in [4]. The substance obtained boiled at 130-132° (3 mm). Hydrogenation of this substance in methanol over palladium on chalk yielded 3,4,7-trimethyloct-5-ene-3,4,7-triol (VII) with b.p. 127-129° (3 mm).

Dehydration of 3,4,7-trimethyloct-5-ene-3,7-diol-4-ol- O^{18} (VII). A mixture of 18 g of the substance, 7 g of $KHSO_4$, and a small amount of hydroquinone was heated to 130°. Water distilled at this temperature, and it was washed with ether, distilled, and sealed in an ampoule.

In 0.05 g of the water isolated was dissolved 0.048 g of potassium carbonate. After the isotopic exchange, the potassium carbonate was treated as described above, and the CO_2 liberated during decomposition was found to contain 0.23% of O^{18} . The calculated O^{18} content of the water examined was 0.24% (Table 2, experiment 7). Consequently, the labeled hydroxyl of the given triol sample, which was in position 2, was not involved in the elimination of the first water molecule.

The reaction products were diluted with ether, dried with potassium carbonate, and distilled. Two fractions were collected: 1st, b.p. 52-54° (8 mm), the product of elimination of two water molecules from the triol, yield 1.1 g; 2nd, b.p. 72-74° (8 mm), n_D^{20} 1.4556, the product of elimination of one water molecule from the triol (not weighed or dehydrated further).

5-Methyl-2-(1-hydroxycyclopentyl)-hex-3-en-2-ol- O^{18} -5-ol (VIII)

1-Acetylcyclopentanol containing O^{18} in the carbonyl was obtained by treating 29 g of acetylcyclopentanol with 5.8 g of 6.1% H_2O^{18} in the presence of 0.05 g of KOH in a thermostat at 70°. Heating was stopped after 2 hr due to appreciable tar formation, and the flask with the mixture was kept at 20° for a further 40 hr. The acetylcyclopentanol containing labeled oxygen in the carbonyl was separated from the water, dried over Na_2SO_4 , and distilled. It was diluted 1.5-fold with unlabeled hydroxy ketone and used for synthesis.

5-Methyl-2-(1-hydroxycyclopentyl)-hex-3-yn-2-ol- O^{18} -5-ol was synthesized as previously. We obtained a fraction with b.p. 151-153° (3 mm), corresponding to a tertiary trihydric acetylenic alcohol. Hydrogenation over palladium in methanol yielded 5-methyl-2-(1-hydroxycyclopentyl)-hex-3-en-2-ol- O^{18} -5-ol with b.p. 150-152° (3 mm).

Dehydration of 5-methyl-2-(1-hydroxycyclopentyl)-hex-3-en-2-ol- O^{18} -5-ol. A mixture of 20 g of triol, 10 g of $KHSO_4$, and traces of hydroquinone was heated to 120°. The water was separated and analyzed.

In 0.05 g of the water isolated was dissolved 0.031 g of potassium carbonate. After isotopic exchange, the potassium carbonate was isolated and decomposed with sulfuric acid. The CO_2 liberated contained 0.4% of O^{18} . The O^{18} content of the water examined, calculated from Eq. (2), was 0.50% (Table 2, experiment 5).

The distilled dehydration products were dried with potassium carbonate and distilled to give two fractions: 2nd, b.p. 99-100° (8 mm), n_D^{20} 1.4826, 12 g, and the 1st b.p. 73-74° (7.5 mm), 3.5 g, the dehydration products of the 2nd fraction, 2,2-dimethyl-5-methylene-5-spirocyclopentanedihydropyran.

The second fraction corresponded in properties to the substituted dihydropyranol obtained previously and described in the literature.

Dehydration of second fraction with b.p. 99-100° (8 mm). A mixture of 12 g of substance, 10 g of KHSO_4 , and traces of hydroquinone was heated to 180°. The dehydration products distilled, and together with the water liberated they formed an emulsion. The latter was centrifuged and the aqueous layer washed with ether and distilled. The layer of reaction products was diluted with ether, dried with potassium carbonate, and distilled. It was mainly a fraction with b.p. 73-74° (7.5 mm), n_D^{20} 1.4797 (i.e., it corresponded to the first fraction).

The water liberated was collected and analyzed. In 0.045 g of this water was dissolved 0.049 g of potassium carbonate. After isotopic exchange, the latter was isolated and decomposed with sulfuric acid and by mass spectrographic analysis the CO_2 liberated was found to contain 1.1% of O^{18} . The O^{18} content of the water examined, calculated from Eq. (2), was 1.5%.

Thus, the labeled hydroxyl of the triol, lying in position 2, was completely retained in the products of the first dehydration of the triol, i.e., the high-boiling fraction, further dehydration of which yielded water with labeled oxygen.

Check of procedure for determining O^{18} content of water. A 0.05-g sample of water containing 6.1% of H_2O^{18} was allowed to exchange with 0.048 g of K_2CO_3 . Mass spectrographic analysis showed that the carbon dioxide obtained by decomposition of this sample of potassium carbonate contained 4.4% of O^{18} which, according to Eq. (2), corresponds to 5.9% of O^{18} in the water examined (Table 2, experiment 1).

A 0.05-g sample of distilled natural water was allowed to exchange with 0.04 g of K_2CO_3 . The O^{18} content of the carbon dioxide obtained by decomposition of the potassium carbonate was 0.2%, which corresponds to the natural ratio of $\text{O}^{18}/\text{O}^{16}$ in the water examined (Table 2, experiment 2).

SUMMARY

1. Some acetylenic and ethylenic 1,2,5-triols with O^{18} in the hydroxyl in position 2 or 5 were prepared.
2. The stepwise dehydration of the triols obtained by potassium bisulfate was studied.
3. We unequivocally confirmed the previous conclusion that the dehydration products of ethylenic glycerols are substituted dihydropyrans.

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CYCLIZATION OF ANALOGS OF PSEUDOIONONE AND CITRAL

S. M. Makin, V. B. Mochalin, and D. V. Nazarova

Moscow Institute of Fine Chemical Technology

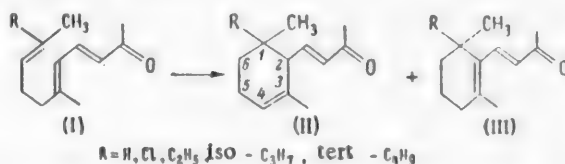
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 5, pp. 1471-1476,

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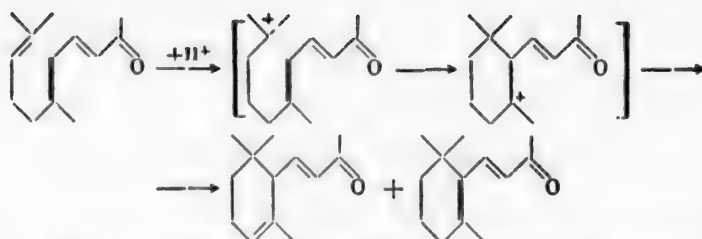
The cyclization of pseudoionone and some of its analogs to α - and β -ionones has been the subject of a considerable number of investigations [1-9], as a result of which it has been found that the cyclization of pseudoionones takes place under the influence of various acids. The ratio of the α - and β -isomers formed depends mainly on the nature of the cyclizing acid. At the present time it has been established that gaseous BF_3 , 60% H_2SO_4 , and H_3PO_4 are specific agents for the cyclization of pseudoionone to α -ionone, but the reaction of pseudoionone with concentrated sulfuric acid leads to the formation of almost pure β -ionone. It has been shown recently that, regardless of the nature of the cyclizing agent, the initial and principal product of the cyclization of pseudoionone is α -ionone, which may be further isomerized to β -ionone [10], depending on the reaction conditions and the nature of the cyclizing agents.

In the present work we investigated the cyclization of some analogs of pseudoionone with various gem-substituents in position 1, which we had prepared previously [11].



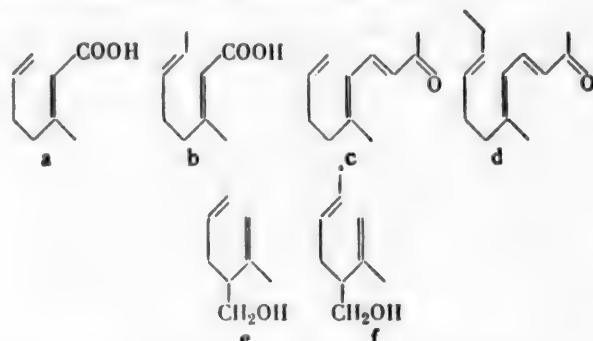
For our study of the cyclization of all the analogs of pseudoionone we chose two standard methods of cyclization. In the first method the cyclization was accomplished with the aid of boron trifluoride at -5° in benzene solution. As has been indicated above, pseudoionone is cyclized by this method to α -ionone. In the second method the analogs of pseudoionone were cyclized by the action of a mixture of concentrated sulfuric and acetic acids at $10-15^\circ$. This method ordinarily is used for the preparation of the purest possible β -ionone. The cyclization products after appropriate treatment (as described below) and distillation were analyzed by means of their ultraviolet absorption spectra. The amount of the α - and β -forms was evaluated from the intensity of the characteristic absorption bands: at 226-229 $\text{m}\mu$ for the α -form and 195-197 $\text{m}\mu$ for the β -form [12]. Furthermore, the individual α - and β -isomers were characterized by the 2,4-dinitrophenylhydrazones and their ultraviolet absorption spectra. The results obtained are presented in Tables 1 and 2, from which it can be seen that the compounds having hydrogen (I, $\text{R} = \text{H}$) and chlorine (I, $\text{R} = \text{Cl}$) as substituents on carbon atom 1 were not cyclized under the chosen conditions.

In an attempt at cyclization with the aid of BF_3 , these compounds were recovered from the reaction unchanged, but the action of sulfuric acid on them resulted in their complete resinification. The failure of the above-mentioned compounds to cyclize can be explained if we start with the idea of an ionic mechanism of cyclization of pseudoionone [3], according to which the pseudoionone molecule adds a proton of the acid (the cyclizing agent) to form a tertiary carbonium ion, which exists in the form of an ion pair with the anion of the cyclizing acid:



The compounds (I, R = H and Cl) are not cyclized because in this case the formation of carbonium ions probably is less advantageous (requires a greater energy of activation).

Similar cases have been noted in the literature [9] in a study of the cyclization of geranic acids (a, b), and also of some analogs of pseudoionone (c, d) and lavandulol (e, f).

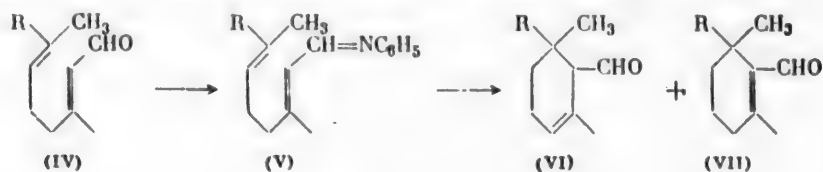


The compounds depicted above proved to be incapable of cyclization.

From Table 1 it is seen that the rest of the analogs of pseudoionone (I, R = C₂H₅, iso-C₃H₇, tert-C₄H₉) were cyclized with the aid of BF₃ presominantly to the α -form (intense absorption band at 229 m μ), although a small amount of the β -form also was present (small band at 295-297 m μ). The pure α -forms were isolated as the 2,4-dinitrophenylhydrazones, and are shown in Table 1.

Cyclization of the analogs of pseudoionone (I, R = C₂H₅, iso-C₃H₇, tert-C₄H₉) with a mixture of concentrated sulfuric and acetic acids (Table 2) did not lead solely to the β -form. The cyclization product contained a considerable amount of the α -isomer (intense absorption bands at 295 and at 226 m μ). The pure β -ionones were isolated as the 2,4-dinitrophenylhydrazones, shown in Table 2.

In this investigation we also studied the cyclization of some analogs of citral that we had prepared previously [13]. The cyclization was accomplished by the action of sulfuric acid on the Schiff bases of the analogs of citral by a method usually employed for the cyclization of natural citral [14].



Analog IV of citral (R = H) and the pseudoionone corresponding to it (I, R = H) proved to be incapable of cyclization because of the reasons discussed above. When sulfuric acid acted on the Schiff base of the chlorine-containing analog (V, R = Cl), splitting out of hydrogen chloride occurred and apparently the reaction resulted in the formation of a cyclic product with b.p. 102-104° (15 mm), n_D²⁰ 1.5320, 2,4-dinitrophenylhydrazone with m.p. 233-234°, λ_{\max} 395 m μ . We did not establish finally the structure of this product. The Schiff bases of the analogs of citral (V, R = C₂H₅ and tert-C₄H₉) were cyclized by sulfuric acid, like natural citral, to a mixture of isomeric cyclocitral in a ratio of α - to β -isomer of approximately 3:1, as was established by the isolation of

TABLE 1

Cyclization of Analogs of Pseudonone with the Aid of BF_3

R	Product of cyclization										2,4-Dinitrophenylhydrazone of α -Form		
	Boiling point (pressure in mm)	n_D^{20}	λ_{max} in $m\mu$	ϵ_{max}	Yield (%)	Found %		Calc. %		λ_{max} in $m\mu$	% N		Melting point
						C	H	C	H		found	calc.	
C_2H_5	105–107° (2.5)	1.5040	229, 295	11800, 1900	56.5	81.67, 81.72	10.80, 10.78	81.50	10.75	376	14.33, 14.59	14.50	156°
iso- C_3H_7	116–119 (3.5)	1.5050	229.5, 297	12910, 1470	62	81.94, 82.06	10.84, 10.90	81.73	10.98	380	14.07, 14.19	14.00	178
tert- C_4H_9	92–94 (0.05)	1.5068	229, 295	11200, 3380	70	82.34, 82.29	10.84, 11.08	82.38	11.18	379	13.59, 13.33	13.53	175–176
H	—	—	—	—	—	Not cyclized		—	—	—	—	—	—
Cl	—	—	—	—	—	The same		—	—	—	—	—	—

TABLE 2

Cyclization of Analogs of Pseudonone with the Aid of Sulfuric Acid

R	Product of cyclization										2,4-Dinitrophenylhydrazone of β -Form		
	Boiling point (pressure in mm)	n_D^{20}	λ_{max} in $m\mu$	ϵ_{max}	Yield (%)	Found %		Calc. %		λ_{max} in $m\mu$	% N		Melting point
						C	H	C	H		found	calc.	
C_3H_5	113–114° (4.5)	1.5184	226, 295	7580, 8890	53.5	81.36, 81.61	10.73, 10.82	81.50	10.75	388	14.56, 14.30	14.50	124°
iso- C_3H_7	118–119 (4)	1.5156	226, 296	8370, 6860	65	81.63, 82.03	10.93, 11.11	81.73	10.98	386	14.26, 14.11	14.00	112
tert- C_4H_9	98–100 (0.3)	1.5082	226, 297	4140, 661	51	82.35, 81.89	11.09, 11.17	82.38	11.18	387	13.24, 13.60	13.53	153–155
H	—	—	—	—	—	Not cyclized		—	—	—	—	—	—
Cl	—	—	—	—	—	The same		—	—	—	—	—	—

TABLE 3

Cyclization of Analogs of Citral

Cyclization product				2,4-Dinitrophenylhydrazones of cyclocitral							
R	Boiling point (pressure in mm)	n_D^{20}	Yield (in %)	α -form (VI)				β -form (VII)			
				Melting point	λ_{max} in m μ	Found	% N calc.	Melting point	λ_{max} in m μ	Found	% N calc.
C ₂ H ₅	100—117° (12)	1.4868	41	142°	361	15.88, 16.20	16.20	129— 129.5°	385	16.29, 16.22	16.20
tert-C ₄ H ₉	58—80 (0.5)	1.4830	32	157— 158	367	15.34, 15.55	14.98	171— 171.5	388	15.21, 15.15	14.98
II Cl	Not cyclized Reacted with evolution of HCl										

the individual α - and β -isomers in the form of their 2,4-dinitrophenylhydrazones and a study of their ultraviolet absorption spectra.

The 2,4-dinitrophenylhydrazones of the analogs of β -cyclocitral have a characteristic absorption band at 385–388 m μ [12], while the 2,4-dinitrophenylhydrazones of the α -cyclocitral have an absorption band at 361 to 367 m μ (Table 3). The mixtures of isomeric α - and β -cyclocitral (VI and VII, R = C₂H₅ and tert-C₄H₉) obtained by cyclization were isomerized by heating with alcoholic alkali [15] to pure β -cyclocitral (VII, R = C₂H₅ and tert-C₄H₉). The analogs of β -cyclocitral thus obtained had a characteristic intense absorption band at 249–250 m μ [16].

EXPERIMENTAL

Cyclization of analogs of pseudoionone under the influence of boron trifluoride. A solution of 10.3 g of 3,7-dimethyldodecatrien-3,7,9-one-11 (I, R = C₂H₅) in 30 ml of dry benzene was saturated at –5° over the course of 20 minutes with gaseous boron trifluoride until there was an increase in weight of 4.2 g. The reaction mixture was kept for 1 hr at 20° and for 30 min at 28°, after which it was poured into 100 ml of an 8% solution of sodium hydroxide with external cooling and stirring. The benzene layer was separated and the aqueous layer was extracted twice with benzene. The combined extract was washed with water, dried with magnesium sulfate, and distilled in vacuum. 5.8 g of 1'-methyl- α -ionone (II, R = C₂H₅) was obtained with a small admixture of 1'-methyl- β -ionone (III, R = C₂H₅) in the form of a slightly yellowish oil with an odor very similar to that of α -ionone (Table 1). The cyclization of the other analogs of pseudoionone given in Table 1 was carried out in a similar manner.

Cyclization of analogs of pseudoionone under the influence of a mixture of sulfuric and acetic acids. To a mixture of 46.5 g of glacial acetic acid and 81.5 g of concentrated sulfuric acid (d 1.84) was added 20.3 g of 3,7-dimethyldodecatrien-3,7,9-one-11 (I, R = C₂H₅), with cooling and stirring over the course of 15 min at 10 to 15°. Stirring was continued at 15° for 30 min more, after which the reaction mixture was poured, with vigorous stirring, into a mixture of 1 liter of ice water and 20 ml of ether. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution, then with water, and dried with sodium sulfate. After the product had been distilled in vacuum, 10.9 g of 1'-methyl- β -ionone (III, R = C₂H₅) was obtained with an admixture of 1'-methyl- α -ionone (II, R = C₂H₅), as established by isolation of the isomeric 2,4-dinitrophenylhydrazones and by the ultraviolet absorption spectra (Table 2). The cyclization of the other analogs of pseudoionone given in Table 2 also was carried out in a similar manner.

Cyclization of analogs of citral. 38.4 g of freshly distilled 3,7,8,8-tetramethylnonadien-2,6-al (IV, R = tert-C₄H₉) in 30 ml of ether was added in small portions to a solution of 18.6 g of aniline in 20 ml of ether, and the mixture was left to stand overnight at room temperature. The water that had separated was removed, and the ether solution of the Schiff base was introduced, over a period of 30 min, with stirring, into a mixture of

200 ml of concentrated sulfuric acid and 10 g of ice that had been cooled to -15° , after which stirring was continued for an hour longer at the same temperature. The reaction mixture was poured onto ice (800 g) and steam distilled. The distillate was saturated with sodium chloride and extracted with ether. The ether extract was dried with magnesium sulfate, and after the ether had been distilled off, the residue was distilled in vacuum. 12.2 g (32%) of a mixture of isomeric cyclocitral (VI and VII, $R = \text{tert-C}_4\text{H}_9$) was obtained. It was established by crystallization and isolation of the individual 2,4-dinitrophenylhydrazones that the ratio of the α -form to the β -form was approximately 1:3 (Table 3). The cyclization of the other analogs of citral shown in Table 3 also was carried out in a similar manner.

Isomerization of mixture of isomeric α - and β -cyclocitral to β -cyclocitral. 7.5 g of the mixture of cyclocitral (VI and VII, $R = \text{tert-C}_4\text{H}_9$) obtained in the preceding experiment was added during a period of an hour, at -5° , to 300 ml of 8% solution of potassium hydroxide in 80% alcohol, and the mixture was allowed to stand for 15 hr in a refrigerator. The reaction mass was poured into 1 liter of cold water and the reaction product was extracted with ether. The ether extract was washed with water and dried with sodium sulfate. After distillation in vacuum, 3.8 g (50%) of 1',1',1'-trimethyl- β -cyclocitral was obtained.

B.p. $53-55^{\circ}$ (0.03 mm), n_D^{20} 1.4898, d_4^{20} 0.9337, M_R_D 60.70; calc. 59.58. λ_{max} 248.325 m μ , ϵ_{max} 9250, 50.9.

Found %: C 80.43, 80.52; H 11.23, 11.13. $\text{C}_{11}\text{H}_{22}\text{O}$. Calculated %: C 80.35; H 11.41.

1'-Methyl- β -cyclocitral was obtained in a similar manner in 69% yield.

B.p. $75-77^{\circ}$ (2.5 mm), n_D^{20} 1.4929, d_4^{20} 0.9324, M_R_D 51.82; calc. 50.34. λ_{max} 250.327 m μ , ϵ_{max} 8350, 51.6.

Found %: C 79.39, 79.35; H 11.03, 11.08. $\text{C}_{11}\text{H}_{20}\text{O}$. Calculated %: C 79.52; H 10.84.

SUMMARY

The cyclization of a number of analogs of pseudoionone and citral having various gem-substituents on the end of the isoprenoid chain has been studied. It has been established that in the absence of even one alkyl substituent, and also in the presence of an electronegative substituent (Cl), cyclization to ionones (or cyclocitral) does not occur. Pseudoionones having various alkyl gem-substituents are cyclized under the influence of BF_3 predominantly to α -ionones, but in the presence of concentrated H_2SO_4 they are cyclized to a mixture of α - and β -ionones.

The Schiff bases of citrals are cyclized by the action of H_2SO_4 to a mixture of α - and β -cyclocitral.

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SYNTHESIS AND CONVERSION OF α -GLYCOLS OF THE ETHYLENE SERIES

VIII. CONVERSION OF 2,3-DIMETHYLPENTENE-4-DIOL-2,3

L. F. Chelpanova, V. A. Kormer, and V. D. Nemirovskii

Lensovet Leningrad Technological Institute

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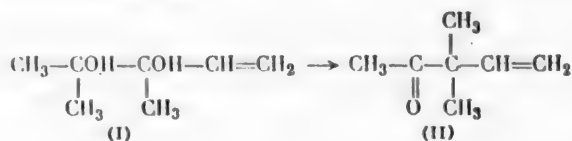
May, 1960

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A. E. Favorskii and his students [1] have shown, through the example of 2,3-dimethylpentene-4-diol-2,3, that unsaturated α -glycols in the presence of strong sulfuric acid are capable of pinacol rearrangement. It was of interest to determine how the analogous α -glycol of the ethylene series (2,3-dimethylpentene-4-diol-2,3) would behave under these conditions on heating with dilute sulfuric acid.

When 2,3-dimethylpentene-4-diol-2,3 (I) (b.p. 89-90° at 15 mm) was heated with 10% H_2SO_4 at 60-70°, a light yellow material with b.p. 107-110° (4 mm) separated out from the acid solution. This material had the empirical formula $C_7H_{12}O$, gave a negative reaction for hydroxyl, decolorized an aqueous solution of potassium permanganate and bromine water, and gave an iodoform test. By treatment with 2,4-dinitrophenylhydrazine, a 2,4-dinitrophenylhydrazone was obtained with m.p. 85-87°.

The formation of an unsaturated ketone can be explained by a pinacol rearrangement of 2,3-dimethylpentene-4-diol-2,3 in the presence of H_2SO_4 .



The infrared absorption spectrum of compound (II) characterized it as an unsaturated ketone. An absorption band with wave number 1710 cm^{-1} corresponded to the frequency of the valence vibration of an unconjugated carbonyl group, and the frequencies 924 and 962 cm^{-1} indicated the presence in the compound of a vinyl group, $-\text{CH}=\text{CH}_2$.

The 2,3-dimethylpentene-4-diol-2,3, which has not been described in the literature, was prepared by hydrogenation of the corresponding acetylenic glycol [1].

Furthermore, when H_2SO_4 acted on the ethylenic glycol, a product with b.p. 120-122° (4 mm) was isolated, the structure of which we were not able to demonstrate.

EXPERIMENTAL

1. Synthesis of Starting Materials

Dimethylethynylcarbinol. 23 g of metallic sodium was introduced into a flask with liquid ammonia over the course of 2 hr, while a strong current of acetylene was simultaneously passed through. 58 g of acetone was added dropwise to the sodium monoacetylide that was obtained. After the mixture had been treated with ice and

water, 60 g of dimethylethynylcarbinol was isolated with b.p. 102-103°, which is in agreement with the data in the literature [2].

Dimethylacetylcarbinol was prepared by the Kucherov reaction. In a flask with a mechanical stirrer were placed 8 g of H₂SO₄, 125 ml of water, and 2 g of mercuric oxide, and the mixture was heated to boiling. While simultaneous steam distillation was carried on, 105 g of dimethylethynylcarbinol was added. The hydroxyketone was salted out from the distillate with potassium carbonate and dried with potassium carbonate. B.p. 140-141° [3]. Yield 105 g (75%).

Trimethylethynylethylene glycol (2,3-dimethylpentene-4-diol-2,3). 23 g of metallic sodium was introduced into a flask with liquid ammonia, with a strong current of acetylene. 92 g of dimethylacetylcarbinol (b.p. 140-141°) was added dropwise to the sodium monoacetylde that was obtained. After the mixture had been treated with ice, water, and ammonium chloride, the material was extracted with ether. After drying and distillation, 58 g (50%) of the glycol was obtained with b.p. 178-180°, d_{20}^{20} 1.103, n_D^{20} 1.4638, which agrees with the data in the literature [1].

2. 2,3-Dimethylpentene-4-diol-2,3

The glycol was prepared by the catalytic hydrogenation of the corresponding α -glycol of the acetylenic series in the presence of colloidal palladium by the usual method [4]. 18.1 g of 2,3-dimethylpentene-4-diol-2,3 was dissolved in 50 ml of alcohol in the presence of 5 mg of colloidal palladium. In 45 min, 3487.8 ml of hydrogen (22°, 767 mm) was absorbed. The catalyst was filtered out and the alcohol was distilled off. The remaining dark brown, oily liquid was distilled in vacuum. 15 g (82%) of 2,3-dimethylpentene-4-diol-2,3 was obtained as a light yellow, oily liquid. With conc. H₂SO₄ it was colored orange. It had a slight moldy odor.

B.p. 89-90° (15 mm), n_D^{20} 1.4600, d_{20}^{20} 0.9660, MR_D 36.72; calc. 37.10.

Found %: C 64.79; H 10.64; OH 34.00. M 128. C₇H₁₄O₂. Calculated %: C 64.61; H 10.77; OH 34.46. M 130.

Action of sulfuric acid of various concentrations on 2,3-dimethylpentene-4-diol-2,3. a) Action of 30% sulfuric acid. When the α -glycol was heated with 30% H₂SO₄ for 2 hr at 60-70°, marked resinification of the reaction mixture was observed, and it was not possible to isolate the individual products.

b) Action of 20% alcoholic sulfuric acid. When the compound in question was treated with 20% alcoholic sulfuric acid at 89-90°, a complex mixture of reaction products was obtained and also 70% of tar, which we could not separate.

c) Action of 10% sulfuric acid. In a flask with a mechanical stirrer were placed 43 g of the ethylenic glycol (b.p. 89-90° at 15 mm) and 300 ml of 10% H₂SO₄, and the mixture was heated for 4 hr on a boiling water bath. In 20 min the solution took on a blue color, and on further heating it became dark brown. At the end of the reaction the acid solution was extracted with ether. The ether extract was washed with sodium carbonate solution and water, and dried with sodium sulfate. After the first distillation in vacuum at 5 mm, three fractions were obtained: 1st, 57-100°, 2 g; 2nd, 100-120°, 10 g; 3rd, 120-140°, 15 g.

When the 2nd and 3rd fractions were redistilled, three fractions were separated: 1st, 70-107° (4 mm), 2.5 g; 2nd, 107-110° (4 mm), 8 g; 3rd, 120-122° (4 mm), 4 g. There was 40% of residue consisting of solid tar.

The first fraction was not investigated because the amount was so small. The second fraction had a camphorlike odor, decolorized an aqueous solution of potassium permanganate, showed the absence of hydroxyls with Grignard reagent and the presence of a carbonyl group with 2,4-dinitrophenylhydrazine, and gave an iodoform test.

B.p. 107-110° (4 mm), n_D^{20} 1.4921, d_{20}^{20} 0.9270, MR 34.65; calc. 34.06.

Found %: C 75.99, H 10.05. M 115. C₇H₁₂O. Calculated %: C 75.00; H 10.71. M 112.

Infrared spectrum: * 780 v.w., 805 av., 896 av., 924 s., 962 s., 1005 v.w., 1031 v.w., 1243 v.w., 1265 v.w., 1325 v.w., 1373 s., 1466 s., 1650 w., 1710 s., cm⁻¹.

* The infrared spectra were obtained with an IKS-14 spectrophotometer with NaCl and LiF prisms and a layer 0.01 mm in depth.

On treatment with 2,4-dinitrophenylhydrazine a bright yellow 2,4-dinitrophenylhydrazone was obtained with m.p. 85-87°.

Found %: C 52.92; H 5.81; N 19.07, 18.58. $C_{13}H_{16}O_4N_4$. Calculated %: C 53.42; H 5.47; N 19.07.

According to its properties and analytical data, compound (II) with b.p. 107-110° (4 mm) was a ketone of the ethylenic series, 3,3-dimethylpenten-4-one-2.

The third fraction with b.p. 120-122° (4 mm) showed the absence of hydroxyls with Grignard reagent and of carbonyl with 2,4-dinitrophenylhydrazine, decolorized bromine water and potassium permanganate solution, and gave a negative iodoform test.

B.p. 120-122° (4 mm), n_D^{20} 1.4875, d_4^{20} 0.9910, M_D 63.85; calc. 63.49.

Found %: C 75.11; H 10.02. M 220. $C_{14}H_{22}O_2$. Calculated %: C 75.00; H 10.71. M 224.

On the basis of the analytical data, it can be assumed that the compound was a condensation product of two molecules of the glycol, with the elimination of two molecules of water. The structure of this compound was not investigated.

Hydrogenation of 3,3-dimethylpenten-4-one-2. 2 g of 3,3-dimethylpenten-4-one-2 was dissolved in 25 ml of alcohol. In the presence of colloidal palladium, 400 ml of hydrogen (18°, 761 mm) was absorbed in 50 min. After the catalyst had been separated out and the solvent had been distilled off, a light yellow, oily material was isolated with b.p. 132-133°, which corresponded to 3,3-dimethylpentan-4-one-2. The semicarbazone of the saturated ketone was obtained with m.p. 137-138° [5].

Found %: N 24.08. $C_8H_{17}ON_3$. Calculated %: N 24.54.

Infrared spectrum: 1060 w., 1107 w., 1162 w., 1231 v.w., 1245 v.w., 1323 v.w., 1375 s., 1437 av., 1692 v.w., 1704 v.s., cm^{-1} .

SUMMARY

1. An α -glycol of the ethylenic series, 2,3-dimethylpentene-4-diol-2,3, which has not been described in the literature, was prepared.

2. It has been shown that when 10% sulfuric acid acts on 2,3-dimethylpentene-4-diol-2,3, a pinacol rearrangement of the glycol takes place with the formation of 3,3-dimethylpenten-4-one-2, which has not been described in the literature.

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CONVERSIONS OF TRIPHENYLMETHANE DYES IN ACID MEDIA

I. DETERMINATION OF BASICITY CONSTANTS OF AMINO GROUPS IN THE CATIONS OF DYES

O. F. Ginzburg and P. M. Zavlin

Lensovet Leningrad Technological Institute

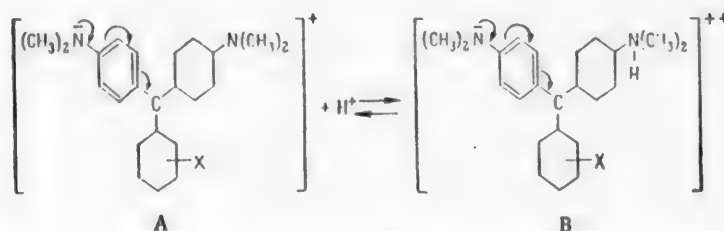
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The values of the hydrolysis constants of dyes of the malachite green group depend to a considerable extent on the nature and the position of the substituent X present in the phenyl ring, which does not contain a dimethylamino group [1,2]. In order to investigate further the relationship between the structure and the acid-base properties of the triphenylmethane dyes, we considered it of interest to trace the connection between the nature of the substituent X and the value of the basicity constants of the dimethylamino groups.

It is well known that in acid media the singly charged cations of the diaminotriphenylmethane dyes are practically instantaneously converted to the more highly colored doubly charged ions [3]. This conversion can be expressed by the following equation:



This equilibrium has recently been studied for malachite green itself [4]. An investigation that we carried out of acid solutions of dyes of the malachite green group, in which the substituents X are in the meta- and para-positions to the central carbon atom showed that the doubly charged cations B that are formed from these dyes,

like the doubly charged cations of malachite green, are unstable and gradually disappear. This occurrence is characterized by a shift of the above equilibrium, in connection with which the concentration of singly charged cations in the solution also gradually decreases. In Fig. 1 the values of the optical densities are given for some of the acid-buffered dye solutions that we studied, at λ_{\max} characteristic of the singly charged cations, at intervals of 4, 8, 12, and 16 minutes after the moment of preparation of the solutions. The doubly charged cations B have practically no absorbing capacity at the values of λ_{\max} for the singly charged cations A.

Extrapolating these values to time $t = 0$, we obtained values for the optical densities (D_0) which also were used for the calculation of the basicity constants of the dimethylamino groups in the cations of the dyes of the malachite green group. In contrast to the above-described solutions, the acid solutions of the dyes of the malachite green group in which the substituents X were in the ortho-position to the central carbon atom did not change in color in the same interval of time. As an example, the corresponding data are given for several dyes in Fig. 2.

TABLE 1

Basicity Constants of Dimethylamino Groups of Dyes of the Malachite Green Group

Expt. No.	X	$K_b \cdot 10^{11}$
1	p-NO ₂	4.0
2	m-NO ₂	5.0
3	m-NO ₂ o-CH ₃	7.9
4	o-NO ₂	10.0
5	o-Cl	7.9
6	m-Cl	10.0
7	p-Cl	12.6
8	p-SO ₃ H	15.8
9	H	20.0, 23.0*
10	m-CH ₃	20.0
11	p-CH ₃	20.0
12	o-CH ₃	31.6
13	o-SO ₃ H	25.1

TABLE 2

Relation of Optical Density and pH in Solutions of Dyes

Expt. No.	Name of compound	D_{\max}	pH	D_4	D_5	D_6	D_{11}	D_{12}	D_9	pK _a
1	2	3	4	5	6	7	8	9	10	
1	Picrate of bis(p-dimethylamino-phenyl)-p-nitrophenylcarbinol [6] 0.5 ml, 20 mm, 620 mμ	0.640	1.1, 1.49	0.316, 0.418	0.246, 0.330	0.187, 0.250	0.138, 0.191	0.412, 0.530	13.4, 13.4	
2	Picrate of bis(p-dimethylamino-phenyl)-m-nitrophenylcarbinol [6] 0.3 ml, 20 mm, 620 mμ	0.680	1.1, 1.49	0.340, 0.476	0.252, 0.427	0.200, 0.370	0.159, 0.316	0.425, 0.546	13.3, 13.3	
3	Picrate of bis(p-dimethylamino-phenyl)-o-nitrophenylcarbinol 0.8 ml, 120 mm, 620 mμ	0.712	0.422, 1.1	0.110, 0.283	0.110, 0.283	0.110, 0.283	0.110, 0.283	0.110, 0.283	12.9, 12.9	
4	Turkish blue BB (By) 0.3 ml, 20 mm, 620 mμ	0.625	1.48, 1.84	0.450, 0.540	0.450, 0.540	0.450, 0.540	0.450, 0.540	0.450, 0.540	13.1, 13.1	
5	Bis(p-dimethylaminophenyl)-p-chlorophenylcarbinol [7] 0.1 ml, 120 mm, 620 mμ	1.16	1.1, 1.86	0.316, 0.760	0.200, 0.629	0.123, 0.549	—	0.490, 0.910	13.0, 12.9	
6	Picrate of bis(p-dimethylamino-phenyl)-m-chlorophenylcarbinol [7] 0.2 ml, 50 mm, 620 mμ	0.607	1.1	0.200	0.141	—	—	0.282	13.0	

Expt. No.	Name of compound	D_{\max}	pH	D_5	D_6	D_7	D_8	D_9	pK _a
1	2	3	4	5	6	7	8	9	10
7	Picrate of bis(p-dimethylamino-phenyl)-o-chlorophenylcarbinol [8] 0.3 ml, 50 mm, 620 m μ	1.33	1.1	0.680	0.680	0.680	0.680	0.680	13.1
8	p-Sulfomalachite green [2] 1.0 ml, 20 mm, 620 m μ	0.450	1.48, 1.84	0.203, 0.288	0.173, 0.257	0.145, 0.234	0.121, 0.209	0.245, 0.320	12.8, 12.8
9	Malachite green hydroiodide [9] 0.1 ml, 20 mm, 613 m μ	0.667	1.48, 1.84	0.250, 0.355	0.178, 0.296	0.129, 0.240	— 0.200	0.346, 0.440	12.7, 12.7
10	Picrate of bis(p-dimethylamino-phenyl)-m-tolylcarbinol [2] 0.2 ml, 50 mm, 615 m μ	1.89	1.55, 1.84	0.740, 1.000	0.538, 0.832	0.398, 0.660	0.295, 0.550	0.955, 1.25	12.7, 12.7
11	Picrate of bis(p-dimethylamino-phenyl)-p-tolylcarbinol [2] 0.2 ml, 20 mm, 615 m μ	0.723	1.55, 1.84	0.276, 0.437	0.200, 0.356	0.144, 0.282	0.109, 0.230	0.380, 0.513	12.7, 12.7
12	Picrate of bis(p-dimethylamino-phenyl)-o-tolylcarbinol [2] 0.2 ml, 50 mm, 618 m μ	2.36	1.48	0.94	0.94	0.94	0.94	0.94	12.5
13	o-Sulfomalachite green [2] 0.5 ml, 20 mm, 630 m μ	0.652	1.48, 1.84	0.274, 0.420	0.274, 0.420	0.274, 0.420	0.274, 0.420	0.274, 0.420	12.6, 12.6

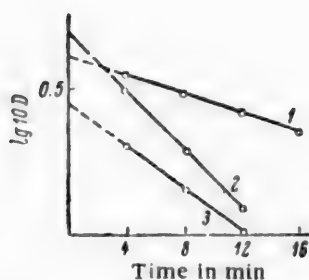


Fig. 1. Change of optical density of solutions of dyes with pH 1.1: 1) picrate of bis(p-dimethylaminophenyl)-p-nitrophenylcarbinol; 2) picrate of bis(p-dimethylaminophenyl)-m-nitrophenylcarbinol; 3) picrate of bis(p-dimethylaminophenyl)-p-chlorophenylcarbinol.

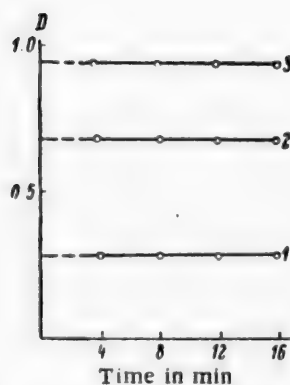


Fig. 2. Optical density of solutions of dyes: 1) picrate of bis(p-dimethylaminophenyl)-o-nitrophenylcarbinol; 2) picrate of bis(p-dimethylaminophenyl)-o-chlorophenylcarbinol; 3) picrate of bis(p-dimethylaminophenyl)-o-tolylcarbinol; pH of solutions 1 and 2: 1.1; 3: 1.48.

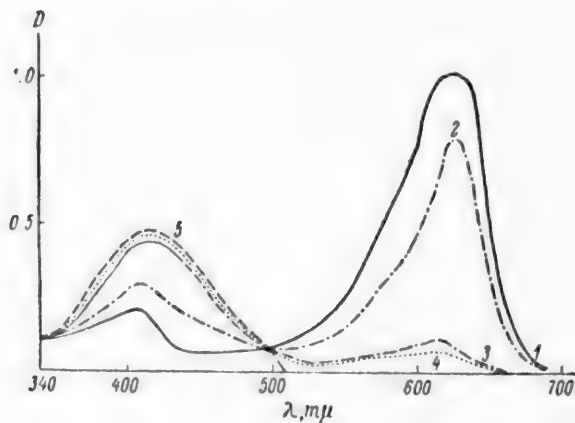


Fig. 3. Absorption spectra of solutions of o-sulfomalachite green with pH: 1) 6.86; 2) 1.81; 3) 0.42; 4) 0.19; 5) 0.13.

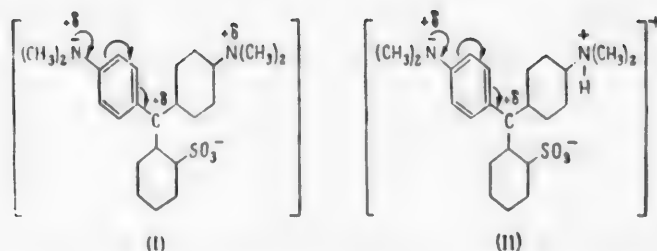
TABLE 3

Optical Density of Solutions of o-Sulfomalachite Green and Their Ion Content

pH	D		% of ions contained	
	630	410	(I)	(II)
6.86	1.22	0.214	100.0	0
1.81	0.797	0.298	65.3	34.7
0.42	0.105	0.450	8.6	91.4
0.19	0.068	0.458	5.6	94.4
0.13	0	0.472	0	100.0

Thus, the presence of a substituent in the doubly charged cation in the ortho-position to the central carbon atom imparts stability to it and slows down or, in general, eliminates further conversion. This conclusion is confirmed also by data obtained in a study of the spectral characteristics of these dyes. Thus, for example, in Fig. 3 the absorption spectra are given for solutions of o-sulfomalachite green of different pH.

The presence in Fig. 3 of an isobestic point shows that, in the solutions investigated, there were no derivatives of o-sulfomalachite green other than the ions (I) and (II).



Having in mind the above-mentioned stability of cations of type B which contain substituents in the ortho-position to the central carbon atom, it must be recognized that in instances where it is desired to employ triphenylmethane dyes as indicators for the characterization of acid solutions, it is necessary to use not malachite green itself, as has been recommended in the literature [5], but a derivative of it with a substituent in the ortho-position.

On the basis of the data given in the experimental section, we computed the basicity constants of the dimethylamino groups in a series of dyes of the malachite green group. The values of these constants are given in Table 1.

Inspection of the data in Table 1 shows that the basicity constants of the dimethylamino groups in dyes of the malachite green group differ from one another comparatively little. However, it can be noted that electron-accepting substituents, in contrast to electron-donor substituents, in most cases decrease the basicity of the dimethylamino groups.

EXPERIMENTAL

The picrate of bis(p-dimethylaminophenyl)-o-nitrophenylcarbinol was prepared in a manner similar to the synthesis of the picrate of bis(p-dimethylaminophenyl)-m-nitrophenylcarbinol [6]. Turkish blue BB was used in the form of a technical sample. All of the rest of the dyes were prepared according to the information given in the literature.

Determination of basicity constants of amino groups in cations of dyes of the malachite green group. To 25.0 ml of buffer solution was added several tenths of a milliliter of a solution of the dye in acetone ($c \sim 10^{-3}$ mole/liter). The optical density of the solution was measured with a Koenig-Martens spectrophotometer at 18–2°, at intervals of 4, 8, 12, and 16 min after preparation of the solution; the values obtained in this way are given in Table 2, in columns 4, 5, 6, and 7. In column 1 are given the names of the compounds, and also the number of milliliters of the solution added to the buffer solution, the thickness of the layer of the solutions investigated, and the wavelength at which the optical density was measured.

The basicity constants of the amino groups in the cations of the dyes were calculated by formula (1):

$$pK_0 = pK_w - pH + \lg \frac{\alpha}{1-\alpha}, \quad \text{where} \quad \alpha = \frac{D_0}{D_{\max}}. \quad (1)$$

D_0 characterizes the optical density of the equilibrium system, consisting only of singly charged and doubly charged conjugated carbonium ions. The value of D_0 (see column 8, Table 2) was found on the basis of the data given in columns 4, 5, 6, and 7 by extrapolation to time $t = 0$.^{*} D_{\max} is the value of the optical density of the solution in which the triarylmethane derivative is present only in the form of the singly charged cation of the dye. D_{\max} for dyes 1–12 was determined in solutions having a pH from 3.8 to 4.2; for dye 13 the value was determined in solutions with pH 7.0.

Absorption spectra of solutions of o-sulfomalachite green. To 25.0 ml of buffer solution was added 2 ml of a solution of the dye in acetone ($c \sim 10^{-3}$ mole/liter). Measurement of the optical density was carried out in a cell with a depth of layer of 10 mm, in an SF-4 spectrophotometer. The absorption spectra are represented in Fig. 3. In Table 3 the values are given for the optical densities of solutions of different pH at wavelengths of 630 and 410 mμ, corresponding to the absorption maxima of o-sulfomalachite green, and also the percentage of ions (I) and (II) contained in these solutions.

^{*}For this purpose we used not the values of D themselves, but their logarithms.

SUMMARY

1. The basicity constants of the dimethylamino groups in dyes of the malachite green group differ comparatively little from the constant of the dimethylamino group in malachite green itself, which is $2 \cdot 10^{-13}$.

2. Derivatives of malachite green that contain substituents in the ortho-position to the central carbon atom are better indicators than malachite green itself because the solutions of these dyes, in contrast to solutions of malachite green and its derivatives with substituents in the meta- and para-positions, are not decolorized in the titration process in acid media.

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SYNTHESES AND CONVERSIONS OF PYRIMIDINE DERIVATIVES

XI. INVESTIGATION OF THE ACTIVITY OF THE METHYL GROUP

IN DERIVATIVES OF 4-METHYL-5-NITROPYRIMIDINE

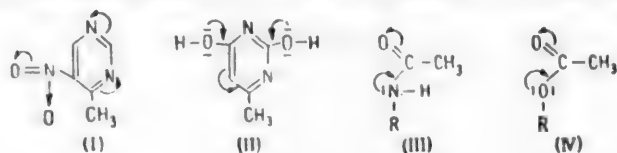
R. S. Karlinskaya and N. V. Khromov-Borisov

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In previous communications it has been shown that the methyl group present in the 4 position of the pyrimidine ring is noticeably activated by its hetero atoms [1]. Its activity is decreased if electron-donor substituents (NH_2 , OH) are introduced into the 2 or the 6 position. The activity of the methyl group is again increased (even in the presence of the substituents mentioned, in the 2 or 6 position) if an electron-acceptor group (NO_2) is introduced into the 5 position or the carbon in position 5 is replaced by nitrogens, for example, 2,6-dihydroxy-4-methyl-5-triazine [2] because of its active methyl group being able to enter into the azo-coupling reaction.

These phenomena are explained in the following manner. The activity of the methyl group (protonization of its hydrogen atoms) increases with an increase in the positive charges (δ^+) on the carbon atoms in positions 2, 4, and 6. These charges are increased as a result of the simultaneous influence of the hetero atoms and the nitro group present in positions 1, 3, and 5, for example (I), and on the other hand, they are decreased under the influence of electron-donor substituents present in the 2 and 6 positions, for example (II).

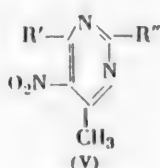


*Original Russian pagination. See C.B. translation.

The amino group has a higher electron-donor capacity than the hydroxyl. This explains the inability of the acetamide and acetanilide (III) to enter into condensations through their methyl group, while derivatives of acetic acid (IV) enter into these reactions (Perkin and Claisen condensations).

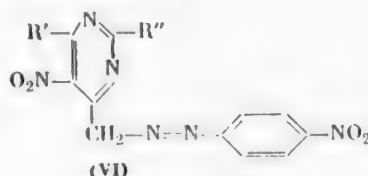
For the same reason, diaminomethyl-S-triazine does not undergo azo coupling, but dihydroxymethyl-S-triazine does [2].

In the present investigation we studied the degree of activity of the methyl group in derivatives of 4-methyl-5-nitropyrimidine (V), in which the electron-donor groups OH and NH₂ were present in 2 and 6 positions. For this purpose we synthesized compounds having the structure (V) (a, b, c, and d), and also isomeric aminochloromethylpyrimidines (V) (e and f).



- | | |
|-------------------------------------|-------------------------------------|
| a: R' = R'' = OH, | d: R' = OH; R'' = NH ₂ , |
| b: R' = R'' = NH ₂ , | e: R' = Cl; R'' = NH ₂ , |
| c: R' = NH ₂ ; R'' = OH, | f: R' = NH ₂ ; R'' = Cl. |

All of these compounds were subjected to the action of p-nitrodiazobenzene, and their ability to enter into azo coupling with it was investigated. The reaction was carried out in acetic acid medium in the presence of sodium acetate. In the first three instances (Va, b, and c) azo coupling took place. The azo compounds having the structures (VIa, b, and c) were formed.

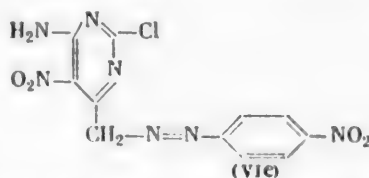
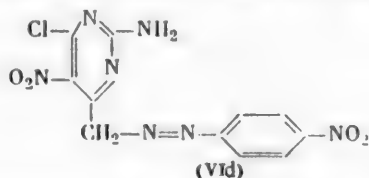


- | |
|-------------------------------------|
| a: R' = R'' = OH, |
| b: R' = R'' = NH ₂ , |
| c: R' = NH ₂ ; R'' = OH, |
| d: R' = OH; R'' = NH ₂ . |

Only the 2-amino-6-hydroxy-4-methyl-5-nitropyrimidine (Vd) was incapable of entering into the azo coupling reaction.

The different activity of the methyl group in the isomeric compounds (Vc) and (Vd and Ve) is explained by the fact that the 2 and 6 positions in the pyrimidine ring are not equivalent, and also apparently by the fact that the possibility of forming an intramolecular hydrogen bond with the nitro group is different in the presence of the amino group (Vc) and of the hydroxyl group (Vd). Compounds (Va, Vb, and Vc) enter into the azo coupling reaction with different degrees of ease; the reaction takes place most easily with the dihydroxy derivative (Va). In this case, the azo compound is formed at room temperature in good yield (70%). The diamino derivative (Vb) reacted with the most difficulty: To carry the reaction to completion it was necessary to heat the reaction mixture; the yield of azo product was 50%.

We also studied the capacity for azo coupling of the isomeric chloroaminomethylnitropyrimidines (Ve and Vf). It appeared that both of these compounds react very easily with p-nitrodiazobenzene. The reaction takes place both in acetic acid medium and in mineral acids. As a result of the very slight electron-donor capacity of chlorine, and the impossibility of its reaction with the neighboring nitro group by way of a hydrogen bond, the methyl groups in compounds (Ve and Vf) were very highly active.



In the azo compounds (VIe and Vf) that were obtained the chlorine was very labile and could be easily replaced by a hydroxyl group. This reaction took place especially easily in compound (VIe): On prolonged standing (20 hr) of the reaction mixture in acetic acid solution at room temperature, complete replacement of the chlorine by hydroxyl took place and the azo compound (VIc) was formed, which could not be obtained by azo

coupling of compound (Ve). In hydrochloric acid solution the hydrolysis of the chlorine and its replacement by the hydroxyl group took place in 3-3.5 hr. Replacement of the chlorine by the ethoxyl group took place in a very short period (5 min) of boiling the compound (Vie) in anhydrous alcohol. To identify the azo compound (Vid) we acetylated it by boiling it with acetic anhydride. The acetylation led to an elevation in color (from red-brown to orange). The acetylated derivative obtained crystallized well from acetic anhydride, had m.p. 292°, and agreed in analytical data with 2-acetamido-6-hydroxy-4-(p-nitrophenylazomethyl)-5-nitropyrimidine.

In the azo compound (Vif) the chlorine was somewhat less labile: To replace it by the ethoxyl group it was necessary to boil the compound for a longer time (35-40 min) with anhydrous alcohol. Replacement of the chlorine by hydroxyl also took place considerably more slowly: The azo coupling product of compound (Vf), which was filtered off from the reaction solution after 20 hr standing at 16-18°, was almost pure 2-chloro-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine (Vif), a dark red crystalline compound with m.p. 290-295° (decomp.). Not less than 48 hr was required to convert compound (Vif) under these conditions almost completely to the above-described compound (Vic). The replacement of chlorine by hydroxyl in this compound (Vif) could also be accomplished by dissolving it in concentrated sulfuric acid and subsequently pouring the solution onto ice.

The azo compound (Vic) obtained by hydrolysis of compound (Vif), and also by azo coupling of compound (Vc), formed an orange-colored monoacetyl derivative with m.p. 267° when it was heated with acetic anhydride. Upon longer heating with acetic anhydride this compound was converted to the light yellow diacetyl derivative with m.p. 220° (from acetic anhydride). In this case also the introduction of acetyl groups was accompanied by an elevation in color (from red to orange, and further to yellow). We should suppose that in the diacetyl derivative the two acetyl groups replace the two hydrogen atoms in compound (Vic) in the amino group that is present in position 6, since it is well known that hydroxypyrimidines containing hydroxyl groups in the even-numbered positions of the heterocycle, as a rule, are not changed on heating with acetic anhydride. The yellow diacetyl derivative easily split out one acetyl group: On heating with 3% aqueous NaOH solution for 5 min at 50° it was converted to an orange monoacetyl derivative; further hydrolysis of the latter could not be brought about.

The inability to convert compound (Vid) to the diacetyl derivative is apparently associated with the fact that 2-amino derivatives of the pyrimidine series are less basic than 6- (or 4-) amino derivatives [3].

In the original isomeric chloroaminomethylnitropyrimidines (Ve and Vf) the chlorine is somewhat less labile than in the corresponding azo compounds (Vic and Vif); however, here also the chlorine in position 6 proved to be considerably more labile than the chlorine in position 2. Thus, for example, 2-chloro-6-amino-4-methyl-5-nitropyrimidine can be recrystallized from alcohol, while 2-amino-6-chloro-4-methyl-5-nitropyrimidine loses chlorine even on short heating in alcoholic solution.

The higher lability of the chlorine in position 6 (or 4) of the pyrimidine heterocycle in comparison with position 2 is in agreement with the higher activity of the methyl group in position 6 (or 4) in comparison with position 2 [4]. It should be pointed out that in one investigation data were adduced on the greater activity of the 2-methyl derivative of pyrimidine in comparison with the 6 (or 4) methyl derivative [5]. However, these data were refuted by other authors [4].

EXPERIMENTAL

Preparation of 4-(p-nitrophenylazomethyl)-5-nitrouracil. 2.2 g of 4-methyl-5-nitrouracil [6] and 4 g of sodium acetate were dissolved by heating in 37 ml of glacial acetic acid. Then there was added to the cooled solution a solution of p-nitrodiazobenzene prepared in the following way: 1.8 g of p-nitroaniline was dissolved in a mixture of 5 ml of concentrated hydrochloric acid and 1.5 ml of water, and was diazotized at 8-10° with a solution of 0.9 g of sodium nitrite in 5 ml of water.

In a few minutes the reaction mixture became colored an intense red and the separation of a red precipitate of the azo compound began, which was filtered off after 20 hr standing at 18-20°. Yield 2.8 g (70%). The precipitate was purified by treating it 6 times with boiling glacial acetic acid solution and filtering it while hot each time. M.p. 265° (decomp.). The compound crystallized from a 400-fold excess of acetic acid (glacial) and dissolved in alkalis with a blue color. When an alkaline solution was acidified, the azo compound separated out in the form of a red amorphous precipitate.

Found %: C 41.2, 41.3; H 3.4, 3.8; N 26.3, 26.2. $C_{11}H_8O_6N_6$. Calculated %: C 41.2; H 2.5; N 26.2.

Preparation of 2,6-diamino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine. 2.2 g of 2,6-diamino-4-methyl-5-nitropyrimidine [7] was dissolved in 37 ml of glacial acetic acid by heating, and 4-5 g of sodium acetate was added. Then there was added to the cooled solution, in small portions and with good stirring, a solution of para-nitrodiazobenzene prepared from 1.8 g of p-nitroaniline (see above). The reaction mixture was carefully heated for 10 min on a water bath at 45-50° while being stirred well. The solution took on a red color and a red precipitate began to separate out. After 4-5 hr the precipitate was filtered off and treated several times with boiling water (80-100 ml each time) to remove the unreacted starting 2,6-diamino-4-methyl-5-nitropyrimidine. Yield 2 g (50%). M.p. 160-170° (decomp.). The compound was analyzed after being boiled twice with 2 N sodium bicarbonate solution (30 ml each time), boiled with water, and treated with 1% hydrochloric acid solution, and again with water. Drying was done in a vacuum desiccator. The crystalline powder was red-lilac in color.

Found %: N 25.20, 25.20. $C_{11}H_{10}O_4N_8$. Calculated %: N 25.20.

1.0 g of the 2,6-diamino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine was dissolved by heating in 200 ml of 15% hydrochloric acid solution. After the solution had cooled, a velvety red-lilac precipitate of the hydrochloride of the azo compound separated out. M.p. 240-245° (decomp.).

Found %: N 31.10, 31.20. $C_{11}H_{10}O_4N_8 \cdot HCl$. Calculated %: N 31.50.

Preparation of 2-hydroxy-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine. 1.8 g of 2-hydroxy-6-amino-4-methyl-5-nitropyrimidine [7] was dissolved in 80 ml of glacial acetic acid by heating. The solution was cooled, and into the suspension that was produced there was poured rapidly, drop by drop, a solution of para-nitrodiazobenzene prepared by diazotizing 1.4 g of p-nitroaniline (dissolved in a mixture of 4 ml of concentrated hydrochloric acid and 2 ml of water) with a solution of 0.72 g of sodium nitrite in 5 ml of water; then 12 g of sodium acetate was added. A red color appeared. After 3-4 min heating on a water bath at 40°, a red precipitate of the azo compound began to separate out. In 1.5 hr the precipitate was filtered off and washed with water. Weight 2.3 g (69%). The compound was insoluble in organic solvents and did not melt up to 300°. It was purified by boiling with 2 N sodium bicarbonate solution (twice with 100 ml portions), with hot filtration each time. The precipitate was then treated with hot water, 2% hydrochloric acid solution, and again with water.

Found %: N 30.40, 30.50. $C_{11}H_9O_5N_7$. Calculated %: N 30.60.

Preparation of 2-hydroxy-6-acetamido-4-(p-nitrophenylazomethyl)-5-nitropyrimidine. 1.3 g of the azo compound obtained in the preceding experiment was heated to boiling for 20 min with 8 ml of acetic anhydride. The separation of a light orange precipitate began very soon (in the heating process). After cooling, the precipitate was filtered off, washed several times with glacial acetic acid, water, and finally with alcohol. Yield 0.4 to 0.5 g. M.p. 267°.

Found %: N 27.00, 26.9. $C_{13}H_{11}O_6N_7$. Calculated %: N 27.10.

Reaction of 2-amino-6-chloro-4-methyl-5-nitropyrimidine with p-nitrodiazobenzene. 2-Amino-6-chloro-4-methyl-5-nitropyrimidine was prepared in the following way: 5.7 g of 2-amino-6-hydroxy-4-methyl-5-nitropyrimidine was added in small portions to a mixture of 29 ml of phosphorus oxychloride and 11 ml of dimethylaniline, and was heated to boiling for 15-20 min. The mixture was cooled and poured onto 100 g of ice with good external cooling. Yield 3.2 g (50%). M.p. about 160°. The identity of the 2-amino-6-chloro-4-methyl-5-nitropyrimidine obtained in this way was proved by converting it (by the action of an alcoholic solution of ammonia) at room temperature to 2,6-diamino-4-methyl-5-nitropyrimidine with m.p. 231°. A mixed sample with known 2,6-diamino-4-methyl-5-nitropyrimidine gave no depression in melting point.

a) Azo coupling in hydrochloric acid solution. 1.0 g of 2-amino-6-chloro-4-methyl-5-nitropyrimidine was dissolved by warming in 20 ml of glacial acetic acid; 3 g of sodium acetate (a known insufficiency, for partial neutralization of the hydrochloric acid) was added to the solution, and after it had cooled there was poured into it with thorough stirring a hydrochloric acid solution of p-nitrodiazobenzene prepared from 0.7 g of p-nitroaniline. In this last process the solution became red. Under these conditions (mineral acid medium) the formation of azo compound was completed in 2 hr. After slight impurities had been filtered off, the reaction solution was diluted with water. When this was done, an amorphous red-brown precipitate separated out, which dissolved in an alcoholic solution of sodium hydroxide with a violet coloration. The precipitate did not contain chlorine. M.p. 280-290° (decomp.). The compound was analyzed after treatment with a hot solution of sodium bicarbonate, water, 2% hydrochloric acid solution, and again water. After this treatment the compound was a crystalline

powder with a red-lilac color. However, we were unable to purify it to an analytically pure condition. 0.4 g of the azo compound obtained in this way was boiled for 25-30 min in 3 ml of acetic anhydride. After the dark reaction solution had cooled, a bright red crystalline precipitate separated out. M.p. 292°.

Found %: N 27.20, 26.90. $C_{13}H_{11}O_6N_7$. Calculated %: N 27.10.

b) Azo coupling in acetic acid solution. 1.0 g of 2-amino-6-chloro-4-methyl-5-nitropyrimidine was dissolved in 20 ml of glacial acetic acid, and 6 g of sodium acetate was added to the solution. A solution of para-nitrodiazobenzene hydrochloride prepared by diazotizing 0.7 g of p-nitraniline was added quickly, drop by drop, with thorough stirring. The solution became intensely red. After 2 hr the impurities were filtered off and the solution was diluted with water. A dark red precipitate of the azo compound separated out, which contained chlorine. Weight 0.2 g. It dissolved in 10% sodium hydroxide solution with a blue coloration. M.p. about 150° (decomp).

The azo compound obtained from 2-amino-6-chloro-4-methyl-5-nitropyrimidine in acetic acid solution lost chlorine upon heating in alcohol solution for 5 min, when it was treated with an alcoholic solution of ammonia at room temperature, and when it was treated with an alcoholic solution of sodium methylate at room temperature.

Reaction of 2-chloro-6-amino-4-methyl-5-nitropyrimidine with p-nitrodiazobenzene. In hydrochloric acid medium: 2.0 g of 2-chloro-6-amino-4-methyl-5-nitropyrimidine [7] was dissolved in 40 ml of glacial acetic acid, 7 g of sodium acetate was added to the solution, and a solution of p-nitrodiazobenzene hydrochloride prepared from 1.4 g of p-nitroaniline was added with stirring. In a few minutes the solution (acid to congo) was scarcely noticeably colored (became rose-colored). It was warmed for 5 min on a water bath at 40-45°. An intense red color appeared. After 18-20 hr the dark red precipitate was filtered off and was treated several times with a warm solution of pyridine, then with hot alcohol to purify it. M.p. 290-295° (decomp.).

Found %: N 28.60, 28.50; Cl 8.80, 8.60. $C_{11}H_8O_4N_7Cl$. Calculated %: N 29.00; Cl 10.30.

The 2-chloro-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine obtained in the preceding experiment was dissolved in concentrated sulfuric acid and the solution was poured onto ice, whereupon a red-orange precipitate separated out, which was filtered off and washed with water. The compound did not contain chlorine. After 10 min boiling in acetic anhydride solution, the orange-colored precipitate was filtered hot. This precipitate melted at 267°, which showed its identity with 2-hydroxy-6-acetamido-4-(p-nitrophenylazomethyl)-5-nitropyrimidine (see above) (mixed sample). The compound dissolved in 10% sodium hydroxide with a violet coloration.

Preparation of the diacetyl derivative of 2-hydroxy-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine. 2.5 g of 2-hydroxy-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine was heated for 35 min with 30 ml of acetic anhydride. The pale yellow precipitate was filtered hot and washed with acetic acid. Weight 1.2 g. It was crystallized from acetic anhydride. M.p. 220°. It was dissolved in 10% sodium hydroxide solution with a violet coloration. The compound contained 1 mole of water of crystallization.

Found %: H_2O 5.0. $C_{15}H_{13}O_7N_7 \cdot H_2O$. Calculated %: H_2O 4.5.

Found %: N 24.60, 24.20. $C_{15}H_{13}O_7N_7$. Calculated %: N 24.30

Hydrolysis of the diacetyl derivative of 2-hydroxy-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine. 1.0 g of the compound obtained in the preceding experiment was dissolved in 10 ml of 3% sodium hydroxide solution and was heated for 5 min at 50°. The solution, after cooling, was acidified with hydrochloric acid, whereupon an orange precipitate of 2-hydroxy-6-acetamido-4-(p-nitrophenylazomethyl)-5-nitropyrimidine separated out. This compound had an m.p. of 267°.

SUMMARY

1. The activity of the methyl group in derivatives of 4-methyl-5-nitropyrimidine containing electron-donor groups (OH and NH_2) in the 2 and 6 positions was investigated. It was established that all of the compounds

* Azo coupling in acetic acid medium leads to the formation of a highly contaminated product. The reaction product proved to be contaminated with tarry impurities even when an excess of the diazonium compound was used.

investigated, with the exception of one, were capable of azo coupling with p-nitrodiazobenzene to form the corresponding derivatives of 4-(p-nitrophenylazomethyl)-5-nitropyrimidine.

2-Amino-6-hydroxy-4-methyl-5-nitropyrimidine did not enter into an azo coupling reaction with p-nitrodiazobenzene.

2. It was found that, in the two isomeric chloroaminomethylnitropyrimidines — 2-chloro-6-amino-4-methyl-5-nitropyrimidine and 2-amino-6-chloro-4-methyl-5-nitropyrimidine — the methyl group has a high activity. When reacted with p-nitrodiazobenzene, both compounds readily form the corresponding 4-(p-nitrophenylazomethyl)-5-nitropyrimidines. The chlorine in these compounds is quite labile: 2-Chloro-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine, and with even greater ease 2-amino-6-chloro-4-(p-nitrophenylazomethyl)-5-nitropyrimidine, were converted in hydrochloric acid solution to 2-hydroxy-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine and 2-amino-6-hydroxy-4-(p-nitrophenylazomethyl)-5-nitropyrimidine, respectively.

3. Upon boiling with acetic anhydride, 2-hydroxy-6-amino-4-(p-nitrophenylazomethyl)-5-nitropyrimidine was converted to the diacetyl derivative. 2-Amino-6-hydroxy-4-(p-nitrophenylazomethyl)-5-nitropyrimidine under these conditions formed only the monoacetyl derivative.

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REACTION OF β -CHLOROVINYL KETONES WITH β -DICARBONYL COMPOUNDS

XII. KETOVINYLATION OF THE ETHYL ESTERS OF α -BENZOYLPROPIONIC AND α -BENZOYLBUTYRIC ACIDS

V. F. Belyaev, M. N. Belokurskaya, and N. K. Kochetkov

Belorussian State University; Institute of Pharmacology and Chemotherapy
of the Academy of Medical Sciences of the USSR

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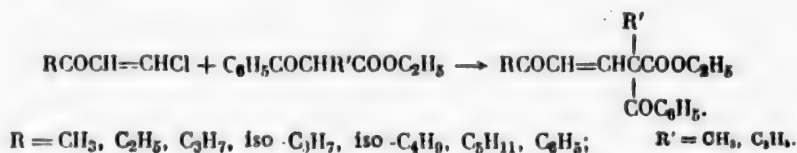
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In previous communications [1,2] it has been shown that β -chlorovinyl ketones react readily with the sodium derivatives of α -alkylacetoacetic esters to form the previously unknown α -alkyl- α -(γ -ketoalkenyl)acetoacetic esters, and this reaction is a simple and convenient method for the preparation of compounds of this class.

It was of interest to broaden the reaction of ketovinylation of β -dicarbonyl compounds with labile hydrogen. We selected as such compounds the ethyl esters of α -benzoylpropionic and α -benzoylbutyric acids, the ketovinylation of which is described in this article. In ethyl- α -benzoylpropionate and ethyl α -benzoylbutyrate there is only one labile hydrogen atom, and it therefore might be expected that normal ketovinylation products would be formed.

*Original Russian pagination. See C.B. translation.

When β -chlorovinyl ketones were reacted with the sodium derivatives of ethyl α -benzoylpropionate and ethyl α -benzoylbutyrate in benzene under conditions similar to those described for α -alkylacetoacetic esters, the ethyl esters of α -(γ -ketoalkenyl-1)- α -benzoylpropionic and α -(γ -ketoalkenyl-1)- α -benzoylbutyric acids were obtained in good yields.



The compounds obtained were high-boiling oils and crystalline materials, stable on storage but easily resinifying upon strong heating, and it therefore was necessary to distill them in a rather high vacuum.

Among the compounds prepared, all of the liquid materials showed a positive exaltation of the molecular refraction (2.10-2.39), which may be well grounded, since these compounds have two systems of conjugated

double bonds $-\text{C}(=\text{O})-\text{CH}=\text{CH}-$ and $-\text{C}(=\text{O})-\text{C}_6\text{H}_5$. According to data reported by Hückel [3], the conjugation of

the carbonyl group with the benzene ring in acetophenone gives an exaltation of +0.78 to the molecular refraction. Furthermore, the β -chlorovinyl ketones in which the carbonyl group is conjugated with a double bond also give a positive exaltation of the molecular refraction [4,5] (for methyl β -chlorovinyl ketone it is +1.14).

The structure of the compounds that we prepared was confirmed by analytical data and also by acid cleavage of the ethyl ester of α -(3-ketobutenyl-1)- α -benzoylbutyric acid, which led to the formation of the ethyl ester of α -(3-ketobutenyl)butyric acid, which was described in one of the previous communications [6], and benzoic acid.

EXPERIMENTAL

Ethyl ester of α -(3-ketobutenyl-1)- α -benzoylpropionic acid. In a three-necked flask equipped with a stirrer, reflux condenser, and dropping funnel, were placed 1.8 g of sodium finely dispersed in xylene, and 100 ml of dry benzene, and over the course of 40 min 18 g of ethyl benzoylpropionate was added dropwise, with stirring. The reaction mixture was heated slightly on a water bath (40°), and after all of the ester had been added it was heated on the water bath at 40-50° for 2 hr more until the sodium had completely dissolved. The reaction mixture was cooled with ice water and, while it was vigorously stirred, a solution of 8 g of methyl β -chlorovinyl ketone in 25 ml of anhydrous benzene was added dropwise over a period of 40 min; then the reaction mixture was heated for 2.5 hr to 40-50°. After the mixture had cooled, 50 ml of water was added, the benzene layer was separated, washed with water (twice, with 40 ml each time), the wash water was extracted several times with ether, the ether extracts were combined with the benzene solution and dried with magnesium sulfate, the solvents were distilled off in a slight vacuum, and the residue was distilled in vacuum from a flask with a low, wide outlet; a fraction with b.p. 140-150° (0.4 mm) was collected.

After redistillation, 12.3 g (59%) of a compound with the following constants was obtained:

B.p. 141-143° (0.3 mm), d_4^{20} 1.1102, n_D^{20} 1.5257, M_R 75.80; calc. 73.70, EMR_D +2.10.

Found %: C 70.12, 70.25; H 6.42, 6.32. $\text{C}_{16}\text{H}_{18}\text{O}_4$. Calculated %: C 70.05; H 6.61.

The ethyl ester of α -(3-ketobutenyl-1)- α -benzoylpropionic acid was a thick, light lemon-colored oil, insoluble in water, miscible with the usual organic solvents. It could be kept for a long time without change.

Ethyl ester of α -(3-ketopenten-1-yl-1)- α -benzoylpropionic acid was prepared in a similar manner from 2.1 g of sodium, 20.5 g of ethyl benzoylpropionate, and 10.7 g of ethyl β -chlorovinyl ketone in 150 ml of anhydrous benzene. Upon distillation in vacuum, with added hydroquinone, a fraction with b.p. 145-155° (0.25 mm) was collected.

After two redistillations, 14.9 g (57.3%) of material was obtained with the following constants.

B.p. 129-131° (0.03 mm), d^{20}_4 1.0944, n^{20}_D 1.5225, MR_D 80.41; calc. 78.31, EMR_D +2.10.

Found %: C 70.89, 71.02; H 7.38, 7.42. $C_{17}H_{24}O_4$. Calculated %: C 70.81, H 7.00.

The ethyl ester of α -(3-ketopenten-1-yl-1)- α -benzoylpropionic acid was a thick, light yellow oil, miscible with the usual organic solvents, insoluble in water. The compound crystallized after a month in colorless plates with m.p. 110°.

Ethyl ester of α -(3-ketohexen-1-yl-1)- α -benzoylpropionic acid was prepared under the same conditions from 1.2 g of sodium, 13 g of ethyl benzoylpropionate, and 7 g of propyl β -chlorovinyl ketone in 140 ml of anhydrous benzene. Upon distillation in vacuum, a fraction was collected with b.p. 136-149° (0.3 mm).

After redistillation, the compound had the following constants: b.p. 133-135° (0.03 mm), n^{20}_D 1.5190. The compound crystallized in the receiver after distillation as colorless plates in the form of polyhedra, m.p. 54° (from ethanol).

Found %: C 71.52, 71.59; H 7.46, 7.69. $C_{18}H_{22}O_4$. Calculated %: C 71.50; H 7.33.

The compound was soluble in benzene, chloroform, petroleum ether, dichloroethane, and ligroin; it dissolved upon heating in acetic acid and ethanol, but was insoluble in water.

Ethyl ester of α -(3-keto-4-methylpenten-1-yl-1)- α -benzoylpropionic acid was prepared from 2.12 g of sodium, 20 g of ethyl benzoylpropionate, and 12 g of isopropyl β -chlorovinyl ketone in 125 ml of anhydrous benzene. Upon distillation in vacuum, a fraction with b.p. 136-144° (0.1 mm) was collected.

After redistillation, 11.2 g (42.1%) of a compound with the following constants was obtained.

B.p. 135-138° (0.06 mm), d^{20}_4 1.0711, n^{20}_D 1.5162, MR_D 85.29; calc. 82.93, EMR_D +2.36.

Found %: C 71.13, 71.32; H 7.48, 7.58. $C_{18}H_{22}O_4$. Calculated %: C 71.50; H 7.33.

The ethyl ester of α -(3-keto-4-methylpenten-1-yl-1)- α -benzoylpropionic acid was a light yellow oil, insoluble in water, soluble in the usual organic solvents.

Ethyl ester of α -(3-keto-5-methylhexen-1-yl-1)- α -benzoylpropionic acid was prepared from 1.8 g of sodium, 17.3 g of ethyl benzoylpropionate, and 11.5 g of isobutyl β -chlorovinyl ketone in 125 ml of dry benzene. Upon distillation in vacuum, a fraction was collected with b.p. 145-152° (0.3 mm).

After redistillation, 10.3 g (41.5%) of compound was obtained with m.p. 18° (from isoamyl alcohol), and with the following constants.

B.p. 145-148° (0.06 mm), d^{20}_4 1.0621, n^{20}_D 1.5148, MR_D 89.79; calc. 87.55, EMR_D +2.24.

Found %: C 71.91, 72.11; H 7.80, 7.85. $C_{20}H_{26}O_4$. Calculated %: C 72.12; H 7.65.

Ethyl ester of α -(3-ketoocten-1-yl-1)- α -benzoylpropionic acid was prepared from 1 g of sodium, 10.35 g of ethyl benzoylpropionate, and 7 g of amyl β -chlorovinyl ketone in 125 ml of anhydrous benzene. Upon distillation in vacuum, a fraction was collected with b.p. 162-165° (0.1 mm). The compound crystallized upon cooling in the receiver as colorless crystals with m.p. 38.5° (from alcohol). Yield 8.1 g (56.3%).

Found %: C 72.77, 72.61; H 8.18, 7.85. $C_{20}H_{26}O_4$. Calculated %: C 72.70; H 7.93.

Ethyl ester of α -(2-benzylethenyl-1)- α -benzoylpropionic acid was prepared from 1.3 g of sodium, 13.5 g of ethyl benzoylpropionate, and 10 g of phenyl β -chlorovinyl ketone in 150 ml of anhydrous benzene. After the solvent was distilled off and the mixture was cooled with a mixture of ice and salt, the compound crystallized.

Colorless crystals with m.p. 63-63.5° (from ethanol). An additional amount of the compound was isolated from the mother liquor of the distillation. Yield 10.1 g (50.3%).

Found %: C 74.93, 75.04; H 6.15, 6.16. $C_{21}H_{20}O_4$. Calculated %: C 74.98; H 6.00.

Ethyl ester of α -(3-ketobutenyl-1)- α -benzoylbutyric acid was prepared from 4.8 g of sodium, 46 g of ethyl benzoylbutyrate, and 20 g of methyl β -chlorovinyl ketone in 300 ml of anhydrous benzene. Upon distillation in vacuum, a fraction was collected with b.p. 136-146° (0.05 mm). Yield 26.5 g (47.4%). After redistillation the compound had the following constants.

B.p. 137-139° (0.06 mm); d_4^{20} 1.0983, n_D^{20} 1.5270, M_R^D 80.70; calc. 78.31, EMR_D +2.39.

Found %: C 71.11, 70.97; H 7.26, 7.07. $C_{17}H_{20}O_4$. Calculated %: C 70.81; H 7.00.

The ethyl ester of α -(3-ketobutenyl-1)- α -benzoylbutyric acid was a thick oil, slightly tinted with a light yellow color.

Acid cleavage of ethyl ester of α -(3-ketobutenyl-1)- α -benzoylbutyric acid. To 6 g of the ethyl ester of α -(3-ketobutenyl-1)- α -benzoylbutyric acid was added, with stirring, a solution of 15 g of ammonium chloride in 50 ml of water, and 20 ml of ammonia (d 0.9) heated to 50°. The temperature was held at 48-50° for 50 min. Then the oily layer was separated and carefully washed with water, and the aqueous layer was extracted with ether. After acidification of the aqueous layer and steam distillation, benzoic acid was isolated with m.p. 121°. The oily material was combined with the ether extracts and shaken with hydrochloric acid solution (1:2). The organic layer was separated, washed well, dried with magnesium sulfate, and distilled in vacuum. 0.7 g of the ethyl ester of α -(3-ketobutenyl-1)butyric acid was obtained.

B.p. 83-85° (1 mm), n_D^{20} 1.4568. Literature data [6]: b.p. 85-88° (1 mm), n_D^{20} 1.4560.

SUMMARY

The reaction of β -chlorovinyl ketones with the ethyl esters of α -benzoylpropionic and α -benzoylbutyric acids has been investigated and has been shown to give high yields (42-65%) of the ethyl esters of α -(γ -ketoalkenyl)- α -benzoylpropionic and -butyric acids, which have not been known previously.

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SYNTHESIS OF CHALCONES FROM β -CHLOROVINYL KETONES

N. K. Kochetkov and V. F. Belyaev

Belorussian State University and Institute of Pharmacology and Chemotherapy
of the Academy of Sciences of the USSR

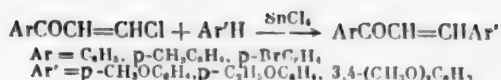
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Existing methods for the synthesis of chalcones (aryl styryl ketones) are based on the condensation of aromatic aldehydes with substituted acetophenones, and are not always convenient because of the unavailability of some of the starting materials. In this paper we present data on a new synthesis of chalcones, based on the condensation of aryl β -chlorovinyl ketones with aromatic compounds. Like their aliphatic analogs [1], the aryl β -chlorovinyl ketones readily react with the ethers of phenols.

*Original Russian pagination. See C.B. translation.



The reaction is most conveniently carried out in benzene solution, with stannic chloride as catalyst. When stannic chloride is added to a benzene solution of the reagents, the evolution of hydrogen chloride is not observed, but a crystalline precipitate soon separates out, which apparently is a molecular compound of stannic chloride with the β -chloroethyl ketone that has been formed, and which decomposes upon further treatment of the reaction mixture with sodium carbonate to produce the chalcone. Obviously, in this case, as in the condensation of aliphatic β -chlorovinyl ketones with phenol ethers [1], the reaction proceeds by way of the addition of the aromatic compound to the double bond of the β -chlorovinyl ketone.

The proposed synthesis of the chalcones obviously is of a rather general nature: The reaction goes both with various aryl β -chlorovinyl ketones (phenyl, p-tolyl, and p-bromophenyl β -chlorovinyl ketones) and with ethers of monoatomic (anisole, phenetole) and polyatomic phenols. The reaction proceeds in a single direction and, in all cases, we have obtained only one compound. To establish the structure of the condensation products obtained, they were oxidized with permanganate in alkaline medium. When the condensation product of phenyl β -chlorovinyl ketone with anisole was oxidized, anisic acid was produced; thus, the condensation took place in the para-position of the aromatic ring, which usually occurs in most cases of substitution in phenol ethers.

When the condensation product of veratrole with p-tolyl β -chlorovinyl ketone was oxidized, veratric acid was produced; thus, in this case, the condensation took place according to the usual mechanism, forming the 3,4-dimethoxy-substituted chalcone.

The chalcones synthesized were obtained by this method in good yields (40-70%) and were nicely crystallized, slightly colored materials. The synthesis proposed here for these compounds has a number of substantial advantages because of its simplicity and the availability of the starting material.

EXPERIMENTAL*

Phenyl-p-methoxystyryl ketone. In a three-necked flask equipped with a stirrer, a reflux condenser with a calcium chloride tube, and a dropping funnel was placed a solution of 30.5 g of phenyl β -chlorovinyl ketone and 20.4 g of anisole in 50 ml of anhydrous benzene. The reaction flask was cooled with a mixture of ice and salt, and 43 g of stannic chloride was added over the course of 2 hr, with vigorous stirring. The reaction mixture gradually took on a raspberry color, hydrogen chloride was not evolved, and a crystalline precipitate separated out. Then the reaction mixture was stirred for 40 min more, and 150 ml of ether and 150 ml of water were added. The ether layer was separated, the aqueous layer was extracted with ether, and the combined ether extracts were repeatedly washed with 5% sodium carbonate solution and dried with calcium chloride, and the ether was distilled off; the residue crystallized as light yellow needles with m.p. 76-77° (from alcohol) [2]. Yield 27 g (61.9%).

Found %: C 80.38, 80.51; H 5.97, 6.18. C₁₆H₁₄O₂. Calculated %: C 80.64; H 5.93.

When 5 g of the compound obtained was oxidized with 30 g of potassium permanganate in 50 ml of 5% sodium carbonate solution, with heating to boiling for 2.5 hr and subsequent acidification of the solution, we obtained anisic acid with m.p. 181-182°, and benzoic acid with m.p. 121°.

Phenyl p-ethoxystyryl ketone was prepared in a similar manner from 25 g of phenyl β -chlorovinyl ketone, 18 g of phenetole, and 35 g of stannic chloride in 50 ml of anhydrous benzene. Crystals were obtained in the form of greenish plates with m.p. 62° (from alcohol) [3], yield 23.5 g (61%).

Found %: C 80.69, 80.77; H 6.27, 6.30. C₁₇H₁₆O₂. Calculated %: C 80.92; H 6.39.

Phenyl 3,4-dimethoxystyryl ketone was prepared from 7 g of phenyl β -chlorovinyl ketone, 6.2 g of veratrole, and 11 g of stannic chloride in 50 ml of anhydrous benzene. Fine yellow needles were obtained with m.p. 81-82° (from alcohol) Yield 4.5 g (40.1%).

Found %: C 76.02, 75.77; H 6.21, 5.93. C₁₇H₁₆O₃. Calculated %: C 76.10; H 6.02.

*G. S. Lomets participated in the experimental portion of the work.

p-Bromophenyl p-methoxystyryl ketone was prepared in a similar manner from 6.1 g of p-bromophenyl β -chlorovinyl ketone, 3 g of anisole, and 7.8 g of stannic chloride in 50 ml of anhydrous benzene. Light yellow needles were obtained with m.p. 142-143° (from alcohol). Yield 4.7 g (60%).

Found %: Br 25.34, 25.33. $C_{16}H_{13}O_2Br$. Calculated %: Br 25.20.

p-Bromophenyl p-ethoxystyryl ketone was prepared from 10 g of p-bromophenyl β -chlorovinyl ketone, 5.2 g of phenetole, and 10.4 g of stannic chloride in 50 ml of anhydrous benzene. Golden yellow needles with m.p. 123.5-124.5° (from alcohol). Yield 8 g (59.9%).

Found %: Br 23.95, 23.95. $C_{17}H_{15}O_2Br$. Calculated %: Br 24.13.

p-Tolyl p-ethoxystyryl ketone was prepared in a similar manner from 7.3 g of p-tolyl β -chlorovinyl ketone, 5.8 g of phenetole, and 13.2 g of stannic chloride in 50 ml of anhydrous benzene. Light yellow plates with m.p. 95.5-96° (from alcohol). Yield 7.5 g (69.9%).

Found %: C 81.22, 81.44; H 6.75, 6.91. $C_{18}H_{18}O_2$. Calculated %: C 81.17; H 6.81.

p-Tolyl 3,4-dimethoxystyryl ketone was prepared in a similar manner from 10.7 g of p-tolyl β -chlorovinyl ketone, 9.9 g of veratrole, and 18.7 g of stannic chloride in 50 ml of anhydrous benzene. Lemon-yellow crystals with m.p. 93.5-94.5° (from alcohol). Yield 10.2 g (61.1%).

Found %: C 76.56, 76.67; H 6.63, 6.55. $C_{18}H_{18}O_3$. Calculated %: C 76.57; H 6.43.

When 5 g of the compound was oxidized with 30 g of potassium permanganate in 50 ml of 5% sodium carbonate solution, veratric acid was obtained with m.p. 180-181° [4] after sublimation.

SUMMARY

A new method has been developed for the synthesis of chalcones (aryl styryl ketones) by the condensation of aryl β -chlorovinyl ketones with phenol ethers (yields 40-70%).

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SYNTHESIS OF RACEMIC N-ACETHOMOMEROQUINENE

M. V. Rubtsov

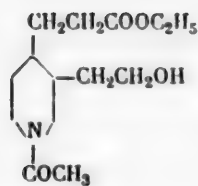
S. Ordzhonikidze All-Union Scientific-Research Chemicopharmaceutical Institute

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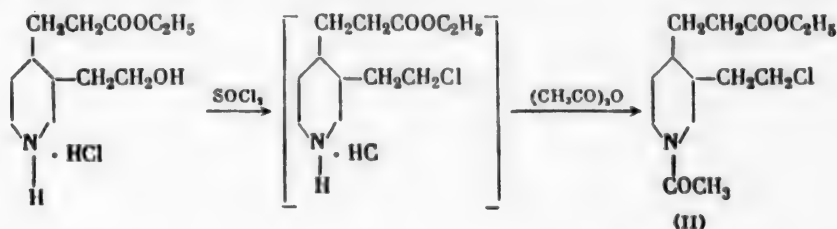
In a previous communication [1] we described the synthesis of 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)-N-acetylpiiperidine (I).



(I)

With compound (I) it appeared to be completely possible to carry out the synthesis of homomeroquinene by using one of the methods appropriate in this case for the production of a double bond.

The use of sulfuric acid to split out water from derivatives of piperidine is known to be accompanied by oxidation of the piperidine ring; the use of phosphorus pentoxide gives high yields of olefin. We therefore chose as our first alternative a method based on the splitting out of hydrogen chloride from the appropriate chloro derivative. The 3-(β -chloroethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine (II) necessary for this was prepared from (I) with the aid of thionyl chloride or from the hydrochloride of 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)piperidine [1] by the following scheme:

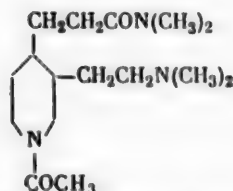


In the latter instance, of especial interest is the acetylation reaction, which gives a good yield by the action of acetic anhydride on the hydrochloride of 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)piperidine, which we did not convert into the base in order to avoid the formation of a pyrrolidine ring.*

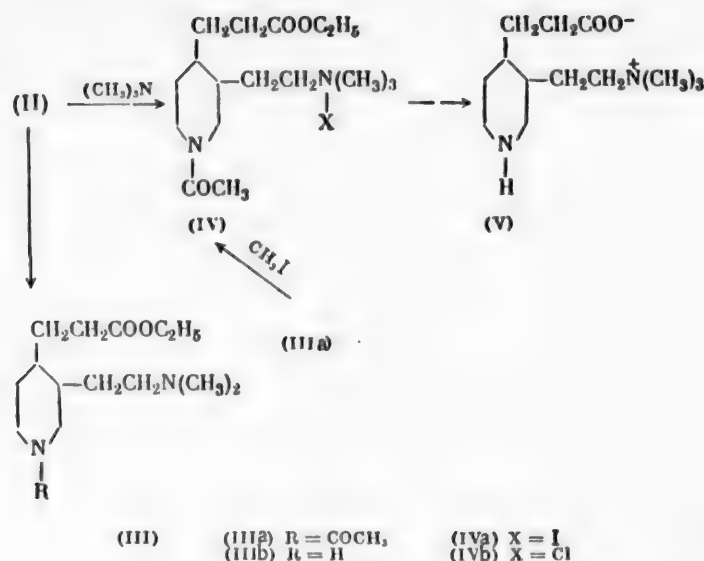
Preliminary experiments showed that when the chloride (II) or the corresponding iodide was treated with an alcoholic solution of potassium hydroxide there was formed, in addition to potassium chloride (or iodide), a caramellike mass that contained only insignificant traces of unsaturated compound. When the caramellike mass was esterified and subsequently acetylated, an oil was obtained with b.p. 90-170° (0.3 mm). This oil was not closely investigated.

Having ascertained the impossibility of producing a vinyl group from the chloroethyl derivative (II), we attempted to prepare homomeroquinene by cleavage of the corresponding quaternary ammonium base. Salts of the quaternary base (IVa, IVb) were prepared either by heating (II) with trimethylamine or by the action of methyl iodide on 3-(β -dimethylaminoethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine (IIIa). (See scheme on following page.)

For the preparation of (IIIa), compound (II) also served as a starting material, being subjected to reaction with dimethylamine. The reaction went easily, but was accompanied by the formation of a considerable amount of the corresponding dimethylamide.



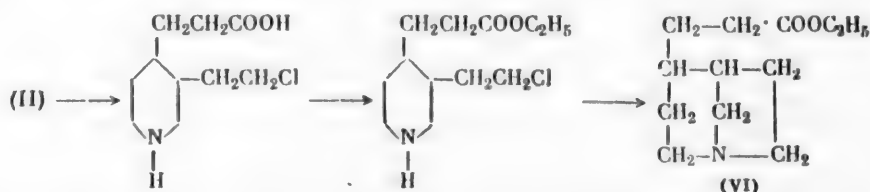
* This reaction may prove to be useful in the case of unstable free bases. We successfully used it for the preparation of 4-(β -bromoethyl)-N-acetylpiperidine from the hydrobromide of 4-(β -bromoethyl)piperidine.



The mixture of the ester (IIIa) and the dimethylamide therefore was saponified with alkali and the saponification product was esterified. The 3-(β-dimethylaminoethyl)-4-(β-carboethoxyethyl)piperidine (IIIb) formed in this process was converted by the action of acetic anhydride to the corresponding N-acetyl derivative (IIIa), which served as the starting material for the preparation of the quaternary salt (IVb). The latter, when treated with moist silver oxide, formed a betaine (V).

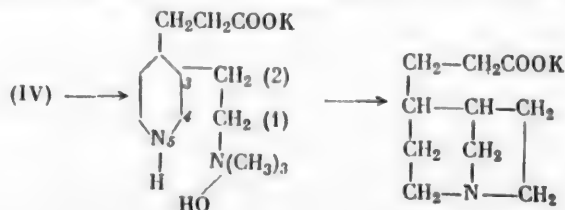
When the quaternary salt (IVa) or (IVb) was fused with 60% potassium hydroxide at 165-170°, trimethylamine was given off and an acid was formed which did not contain either a double bond or a secondary amine group. The acid was converted to the ethyl ester, which corresponded in analysis to the composition of the ethyl ester of β-[1,3-ethylenepiperidyl-(4)]propionic acid (VI).

The structure of this compound was confirmed by direct synthesis of (VI), which was carried out by the following scheme:

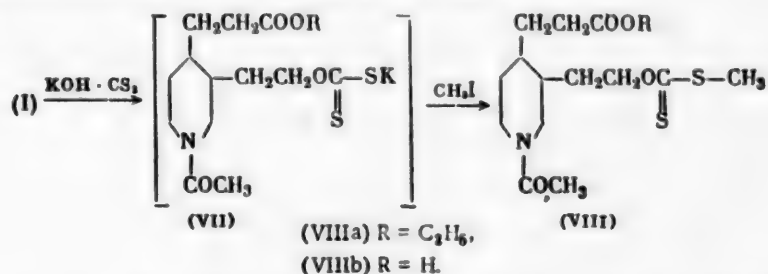


The starting material was 3-(β-chloroethyl)-4-(β-carboethoxyethyl)-N-acetylpiperidine (II), which was converted by hydrolysis with 17% hydrochloric acid to β-[3-(β'-chloroethyl)piperidyl-(4)]propionic acid. The latter was esterified and the 3-(β-chloroethyl)-4-(β-carboethoxyethyl)piperidine formed in this process was cyclized by heating in pyridine solution. The cyclization product proved to be identical with the ethyl ester of the acid obtained by the decomposition of the quaternary base.

Thus it was demonstrated that decomposition of the quaternary base in our case proceeded by an unusual route, and instead of the formation of an unsaturated compound, it led to the appearance of a new five-membered ring. The course of the process apparently can be expressed by the following diagram:

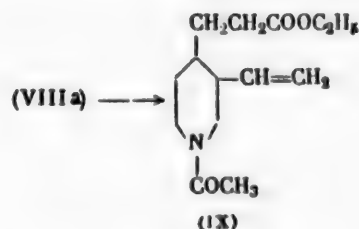


The unusual course of the reaction obviously is associated with the presence on the fifth member of the ring of a labile hydrogen, which splits off with greater ease than the hydrogen located on the second carbon atom. It is quite probable that this reaction is general in nature and can be used for the production of five- and six-membered rings, starting with compounds containing a labile hydrogen in the appropriate positions. Not having obtained an unsaturated compound by the above-mentioned methods, we used the xanthogen method of Chugaev for the production of a double bond. The methyl ester of β -[4-(β '-carboethoxyethyl)-N-acetylpiiperidyl-(3)]-ethylxanthogenic acid (VIIIa) necessary for this purpose was prepared from (I).



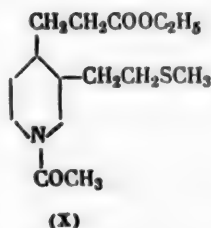
When the potassium salt of the xanthogenic acid (VII) was prepared, partial saponification of the carboethoxy group took place with the formation of the corresponding carboxylic acid. When the reaction mixture was treated with methyl iodide, therefore, a mixture of materials was produced, from which we isolated the methyl ester of β -[4-(β '-carboethoxyethyl)-N-acetylpiiperidine-(3)]ethylxanthogenic acid (VIIIa), the methyl ester of β -[4-(β '-carboxyethyl)-N-acetylpiiperidyl-(3)]ethylxanthogenic acid (VIIIb), and the starting compound (I).

When the methyl ester of β -[4-(β '-carboethoxyethyl)-N-acetylpiiperidyl-(3)]ethylxanthogenic acid (VIIIa) was heated in vacuum at 10 mm to 175°, decomposition occurred with the formation of the ethyl ester of racemic N-acetylhomomeroquinene (IX).



The decomposition process proceeded in more than one way and the reaction product was a mixture of the ethyl ester of N-acetylhomomeroquinene and sulfur compounds, which it was impossible to separate by vacuum distillation. We were able to make a separation because of the fact that the sulfur compounds were considerably more difficultly soluble in water than the ethyl ester of N-acetylhomomeroquinene.

A preliminary study of the sulfur compounds formed in the xanthogenic reaction permitted isolation of a compound that corresponded in analysis to the composition of β -[4-(β '-carboethoxyethyl)-N-acetylpiiperidyl-(3)]ethyl methyl sulfide (X).



When the compound obtained was treated with methyl iodide, a solid light yellow mass formed, which was insoluble in ether and apparently was a sulfonium salt.

EXPERIMENTAL

3-(β -Chloroethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine (II). 9.7 g of 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine (I) was dissolved in 16 ml of absolute benzene. The solution was cooled with cold water, and over a period of 10 min, 3.2 ml of thionyl chloride (about 25% excess) was added, after which the reaction mixture was heated for 4.5 hr at 60-63°. Then the benzene was distilled off in vacuum; the dark red residue was dissolved in 40 ml of chloroform, the chloroform solution was washed with 20 ml of 30% potassium carbonate solution, dried with potassium carbonate, and the solvent distilled off in vacuum. 10.3 g of a dark red oil was obtained. To purify this material from colored contaminants it was mixed with 400 ml of petroleum ether (b.p. 50-70°); the pale yellow solution that was formed was decanted from the dark red caramel-like mass, mixed with carbon, and filtered; then the solvent was distilled off and the residue was distilled in vacuum. 9.2 g (88.7%) of a light yellow oil was obtained which, according to its analysis, was 3-(β -chloroethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine (II).

B.p. 173-175° (0.3 mm), d_4^{20} 1.1360, n_D^{20} 1.4955, M_R 74.44; calc. 74.77.

Found %: C 58.33; H 8.19; Cl 12.41. $C_{14}H_{24}O_3NCl$. Calculated %: C 58.00; H 8.35; Cl 12.29.

The chloride was readily soluble in alcohol, ether, benzene, and chloroform; less soluble in petroleum ether.

A chloride also was obtained from 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)piperidine [1]. For this purpose the hydrochloride of the latter was treated with thionyl chloride (25% excess) in benzene at 60-65° for 4 hr, then the solution was evaporated in vacuum and the residue, which was the hydrochloride of 3-(β -chloroethyl)-4-(β -carboethoxyethyl)piperidine, was heated for 2 hr with an excess of acetic anhydride on a water bath. After the acetic acid and excess acetic anhydride had been distilled off in vacuum, the residue was dissolved in chloroform, the solution was washed with 30% potassium carbonate solution, and the base was isolated and purified as described above. Yield 86%, calculated on the hydrochloride of 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)piperidine.

When the chloride was treated with an alcoholic solution of potassium hydroxide, practically no double bond was formed. Thus, for example, when the chloride was boiled for 3 hours with 15% potassium hydroxide solution in methanol, we obtained, after removal of the excess alkali with the aid of carbon dioxide and evaporation of the filtrate, a caramellike mass which showed only insignificant traces of unsaturated compound when tested with dilute permanganate solution. When the product obtained was esterified and then acetylated, an oil was formed with b.p. 90-170° (0.3 mm).

The corresponding iodide obtained by heating the chloride with sodium iodide in dry acetone behaved similarly.

3-(β -Dimethylaminoethyl)-4-(β -carboethoxyethyl)-N-piperidine (IIIb). A mixture of 3.9 g of 3-(β -chloroethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine, 10.6 g of dimethylamine in 20 ml of methanol, and 2 g of sodium iodide was heated for 5 hr in a sealed tube at 75-80°. When the solution had cooled, it was filtered off from the sodium chloride and the filtrate was evaporated in vacuum. The residue was mixed with acetone, the solution was filtered off from the dimethylamine hydroiodide, and the filtrate was again evaporated in vacuum. The glassy brown mass obtained in this way was dissolved in 2 ml of water, 4 ml of a saturated potassium carbonate solution was added, and the oil that separated out was extracted first with ether (twice with 25-ml portions), and then with chloroform (3 times with 20-ml portions). About half of the separated oil went into ether solution, while the remainder was insoluble in ether, but was readily extracted with chloroform. The extracts were dried with potassium carbonate, the solvents were distilled off, and the residual portion of the solvents was removed in vacuum at 100°. From the ether extract, 1.8 g of a yellow, mobile oil (A) was obtained; n_D^{20} 1.4890.

From the chloroform extract, 2 g of a light brown, thick, only slightly mobile oil (B) was obtained; n_D^{20} 1.510.

Tests showed that when material A was shaken with 15% potassium hydroxide solution for 30 min it went almost completely into solution, while material B dissolved in alkali only when boiled for 1 hr, during which the odor of dimethylamine appeared. Evidently the first compound was an ester and the second was the corresponding dimethylamide.

The two materials were mixed and subjected to saponification with 40 ml of 15% potassium hydroxide solution by boiling for 2.5 hours. Then the solution was evaporated in vacuum to a volume of about 15 ml, acidified, while being cooled, with 17% hydrochloric acid to a slight acid reaction to Congo, and evaporated in vacuum to dryness. The residue was mixed with absolute alcohol, the solution was filtered off from the potassium chloride, and the alcohol was distilled off in vacuum. The residue was dehydrated with the aid of absolute alcohol, and subjected to esterification with 5% alcoholic solution of hydrogen chloride. Upon removal of the alcohol, a glassy light brown mass was obtained, which was the hydrochloride of the ester.

To isolate the free base, the mass obtained was dissolved in 40 ml of chloroform; 5 g of potassium carbonate and 2.5 ml of water were added to the solution, and then the mixture was shaken for 2 hr. Then the chloroform extract was dried with potassium carbonate and the chloroform was distilled off in vacuum. The light brown oil that remained was dissolved in 20 ml of absolute ether, the solution was decanted from the undissolved dark brown tarry mass, the solvent was distilled off, and the residue was dried in vacuum at 70°. Yield 2.6 g (75.4%).

The product was a light yellow mobile oil, readily soluble in water, alcohol, ether, and chloroform, n_D^{20} 1.4825. The material was not vacuum distilled, in order to avoid losses associated with the formation of by-products of a lactam nature.

Found %: N 10.52. $C_{14}H_{23}O_2N_2$. Calculated %: N 10.93.

The compound obtained did not form crystalline salts with picric or hydrochloric acids. When it was treated with acetic anhydride, the N-acetyl derivative (IIIa) was formed as a colorless mobile oil.

B.p. 163-165° (0.3 mm), d_4^{20} 1.0331, n_D^{20} 1.4855, M_R 82.82; calc. 83.08.

Found %: C 64.30; H 9.84; N 9.20. $C_{16}H_{30}O_3N_2$. Calculated %: C 64.38; H 10.14; N 9.39.

β -[4-(β '-carboethoxyethyl)-N-acetylpiiperidyl-(3)]ethyltrimethylammonium iodide (IVa). To a solution of 1.16 g of 3-(β -dimethylaminoethyl)-4-(β -carboethoxyethyl)-N-acetylpiiperidine (IIIa) in 4 ml of absolute alcohol was added 1.1 ml of methyl iodide (heat was evolved). The mixture was refluxed for 2 hr at 60° on a water bath, then the alcohol and excess methyl iodide were distilled off and the residue was dried in vacuum at 90°. 1.73 g of a light yellow, glassy, very hygroscopic mass was obtained, which was readily soluble in water, alcohol, and chloroform. Yield quantitative.

Found %: I 28.4. $C_{17}H_{33}O_3N_2I$. Calculated %: I 28.8.

Trimethylbetaine of β -[3-(β '-aminoethyl)piiperidyl-(4)]propionic acid (V). A solution of 1.53 g of the quaternary salt obtained above in 4 ml of water was mixed with moist silver oxide prepared from 1 g of silver nitrate. The mixture was shaken for 3 hr, then filtered off from the precipitate and the filtrate was evaporated in vacuum to dryness. The light brown residue was mixed with 50% alcohol, filtered off from a small amount of gray sediment, and evaporated to dryness in vacuum on a boiling water bath. 1.05 g of a white, solid, very hygroscopic mass was obtained, which had the appearance of congealed foam and melted at about 80°. The substance was readily soluble in water, alcohol, and chloroform; an aqueous solution showed a neutral reaction to litmus; it did not form crystalline salts with picric or perchloric acids.

This material, which was the trimethylbetaine of β -[3-(β '-aminoethyl)-N-acetylpiiperidyl-(4)]propionic acid, was subjected without further purification to hydrolysis by heating with 6 ml of 17% hydrochloric acid on a boiling water bath for 3 hr. Then the solution was evaporated in vacuum, absolute alcohol was added several times to the residue and then distilled off, after which the residue was dissolved in water and treated with moist silver oxide prepared from 2 g of silver nitrate. 0.8 g of the trimethylbetaine of β -[3-(β '-aminoethyl)-piiperidyl-(4)]propionic acid was obtained as a white mass with a slight yellowish tint, which looked like congealed foam. The material was readily soluble in water, alcohol, and chloroform; it quickly deliquesced in the air.

When an alcohol solution of picric acid was added to an aqueous solution of the compound, a picrate precipitated in the form of a yellow crystalline powder, poorly soluble in hot water and hot alcohol, and moderately so in acetone. When an acetone solution was diluted with an equal volume of ether, yellow nodules of fine needles precipitated; m.p. 225-226°.

Found %: C 42.48; H 4.96; N 15.8. $C_{15}H_{26}O_2N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 42.84; H 4.61; N 16.0.

β -[4-(β -carboethoxyethyl)-N-acetylpiperidyl-(3)]ethyltrimethylammonium chloride (IVb). 2.1 g of 3-(β -chloroethyl)-4-(β' -carboethoxyethyl)-N-acetylpiperidine was mixed with a solution of 2.8 g of trimethylamine in 21 ml of methanol, and the solution obtained was heated in a sealed tube for 10 hr at 100-105°. After the reaction mixture had cooled, it was evaporated in vacuum to a volume of about 4 ml, diluted with 60 ml of ether, and left to stand overnight. The clear ether layer was decanted from the thick yellow mass; the latter was washed with ether and dried in vacuum at 80°. A glassy light brown mass was obtained, which was readily soluble in water, alcohol, and chloroform; it quickly deliquesced in the air. Yield 2.05 g (81%).

Found %: Cl 9.73. $C_{17}H_{33}O_3N_2Cl$. Calculated %: Cl 10.16.

Fusion of quaternary salt with alkali. 1.9 g of the quaternary salt (IVb) prepared above was mixed with a solution of 3.5 g of sodium hydroxide in 2.5 ml of water in a nickel crucible. The mixture was gradually heated in a Wood's metal bath to 165°, and then was stirred for 20 min at 165-175°. From time to time during this process drops of water were added, so that the volume of the reaction mixture remained within the limits 5-6 ml. At approximately 130° the odor of trimethylamine appeared. Upon further heating the evolution of trimethylamine increased, and the homogeneous mass began to separate gradually into two layers: The lower layer was alkali solution, and the upper one organic material. The reaction mixture was cooled to approximately 100-120°, and the organic mass, a semisolid light brown substance, was separated from the alkali, pressed out on filter paper, and dissolved in 3 ml of water. A test with permanganate in the presence of dilute sulfuric acid showed only traces of unsaturated compound; consequently, the reaction followed a different course than had been supposed. The solution of the material that was obtained was neutralized with hydrochloric acid and evaporated to dryness in vacuum. The residue was mixed with absolute alcohol, the solution was filtered off from the inorganic salts, and the alcohol was evaporated in vacuum. The residual glassy mass was esterified with a 4% alcoholic solution of hydrogen chloride. The free base was isolated from the reaction mixture by the usual method, in the form of a colorless mobile oil. The material did not contain a secondary amino group, and was readily soluble in dilute mineral acids and the usual organic solvents. It agreed in analysis with the ethyl ester of β -[1,3-ethylenepiperidine-(4)]propionic acid (VI). Yield 0.52 g (45.2%).

B.p. 98-100° (0.3 mm), d_4^{20} 1.0226, n_D^{20} 1.4792. M_R 58.58; calc. 58.69.

Found %: C 68.45; H 10.07; N 6.82. $C_{12}H_{21}O_2N$. Calculated %: C 68.19; H 10.02; N 6.63.

The picrate formed lustrous yellow prismatic plates (from alcohol); m.p. 133-134°.

As evidence of the structure of the compound obtained, it was synthesized in the following way: 1 g of 3-(β -chloroethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine (II) was boiled with 10 ml of 17% hydrochloric acid for 3 hr. Then the solution was evaporated in vacuum, the residue was dehydrated by repeated addition of absolute alcohol with subsequent removal by distillation in vacuum, after which it was esterified with 4% alcoholic solution of hydrogen chloride. After the alcohol had been distilled off, the residue was dissolved in 2 ml of ice water, made alkaline with concentrated potassium carbonate solution, and the base that separated out was extracted with ether. The extract was shaken for a short time with anhydrous pulverized potassium carbonate; then the ether solution was filtered off and evaporated in vacuum. 0.65 g of light yellow oil was obtained, which was 3-(β -chloroethyl)-4-(β -carboethoxyethyl)piperidine. Since this compound does not give crystalline salts with picric and hydrochloric acids, and is not stable in the form of the base, it was subjected to cyclization without further purification. For this purpose the compound was dissolved in 7 ml of dry pyridine, and the solution was heated to gentle boiling for 2 hr. Then the pyridine was distilled off in vacuum, the residue (0.65 g) was mixed with a saturated solution of potassium carbonate, and the oil that separated was extracted with ether and dried with potassium carbonate. After the ether had been distilled off in vacuum, the residue was distilled in vacuum at 0.3 mm. 0.47 g (64.4%) of a colorless oil was collected, which boiled at 98-100° and exhibited properties [b.p. 98-100° (0.3 mm), n_D^{20} 1.4790, m.p. of picrate 133-134°] identical with those of the ethyl ester of the acid prepared by fusing the quaternary salt with alkali.

Methyl ester of β -[4-(β' -carboethoxyethyl)-N-acetylpiperidyl-(3)]ethylxanthogenic acid (VIIIa). To a solution of 8.86 g of 3-(β -hydroxyethyl)-3-(β -carboethoxyethyl)-N-acetylpiperidine (I) in 20 ml of benzene was added 2.1 ml of carbon bisulfide and the mixture was vigorously shaken for 15 min with a solution of 1.83 g of potassium hydroxide in 1 ml of water. In this process an emulsion was formed at first, and then the reaction mixture separated into two layers: the upper layer, of benzene and the lower, a light yellow, thick oil. 2.6 ml of methyl iodide was added to the reaction mixture, and the mixture was shaken for 15 min more. Methylation

took place very quickly and was accompanied by slight evolution of heat. The methyl ester of the xanthogenic acid that was formed went into solution in the benzene with the simultaneous separation of potassium iodide. A small amount of water was added to the mixture to dissolve the precipitate; then the benzene layer was separated off, washed with water until it gave a neutral reaction to litmus, and the benzene was distilled off in vacuum at 40°. The oil obtained was dissolved in 60 ml of ether, and the ether solution was washed with water 6 times, with 10-ml portions, to remove completely the starting material (the starting material was easily extracted by water from the ether solution). The ether solution was dried with potassium carbonate, the ether was distilled off, and the residue was dried in vacuum (0.3 mm) at 100°. 5.94 g (64%) of the methyl ester of β -[4-(β '-carboethoxyethyl)-N-acetylpiperidyl-(3)]ethylxanthogenic acid (VIIIa) was obtained in the form of a light yellow, thick oil, readily soluble in the usual organic solvents.

d^{20}_4 1.1611, n^{20}_D 1.5379, M_R 97.30; calc. 97.94.

Found %: N 3.93; S 17.00. $C_{16}H_{27}O_4NS_2$. Calculated %: N 3.88; S 17.70.

All the wash water was combined, mixed with 1 ml of concentrated potassium carbonate solution, and extracted with chloroform (extract 1). Then the aqueous solution was acidified with hydrochloric acid to a slightly acid reaction to Congo, and the light yellow mass that precipitated was extracted with chloroform (extract 2). From extract 1 was isolated 1.9 g of the starting material. From extract 2 was obtained 1.63 g (19%) of a light yellow, caramellike mass, which proved, on analysis, to be the methyl ester of β -[4-(β '-carboethoxyethyl)-N-acetylpiperidyl-(3)]ethylxanthogenic acid (VIIIb).

Found %: N 4.29; S 18.40. $C_{14}H_{23}O_4NS_2$. Calculated %: N 4.20; S 19.20.

Ethyl ester of racemic N-acetylhomomeroquinene (IX). 5.61 g of the methyl ester of β -[4-(β '-carboethoxyethyl)-N-acetylpiperidyl-(3)]ethylxanthogenic acid was placed in a Claissen flask and heated in a vacuum at 10 mm on a Wood's metal bath. When the temperature of the bath reached 175°, decomposition began and the pressure rose to 35 mm. In a few minutes the decomposition came to an end and the pressure fell again to 10 mm. To complete the decomposition, the temperature of the bath was gradually increased to 220°; then the system was switched over to the oil pump and the reaction product was distilled off at 0.3 mm on a bath, the temperature of which was gradually raised to 270°. The distillate was redistilled at 0.3 mm. 1.53 g of a colorless thick oil having the unpleasant odor of sulfur compounds was collected. B.p. 165-182°. To separate the ethyl ester of N-acetylhomomeroquinene from the sulfur-containing byproducts, the oil obtained was mixed with 100 ml of water; the aqueous solution was separated off from the insoluble oil and washed 5 times with 20-ml portions of ether. Then the aqueous solution was mixed with 10 ml of saturated potassium carbonate solution, repeatedly extracted with ether, and the extract was dried with potassium carbonate. After the ether had been distilled off, the residue was distilled in vacuum (0.3 mm). 0.37 g (9.4%) of a thick colorless oil was obtained, which boiled at approximately 168-172°. The material did not contain sulfur nor a hydroxyl group; it was readily soluble in water, alcohol, ether, acetone, and chloroform. A solution of the material in dilute sulfuric acid decolorized an aqueous solution of permanganate. This material, according to its analysis, was the ethyl ester of N-acetylhomomeroquinene.

d^{20}_4 1.0438, n^{20}_D 1.4822, M_R 69.17; calc. 69.44.

Found %: C 66.37; H 9.26; N 5.72. $C_{14}H_{23}O_3N$. Calculated %: C 66.36; H 9.16; N 5.53.

The ether extract containing the sulfur compounds was mixed with the water-insoluble oily material, and the ether solution obtained was washed 6 times with 15-ml portions of water to remove completely the ethyl ester of N-acetylhomomeroquinene. Then the ether solution was dried, the ether was distilled off, and the residue was distilled in vacuum.

0.5 g of a colorless oily material was obtained. This material was readily soluble in the usual organic solvents. According to its analysis, it corresponded to the composition of β -[4-(β '-carboethoxyethyl)-N-acetylpiperidyl-(3)]ethyl methyl sulfide (X).

B.p. 181-195° (0.3 mm), d^{20}_4 1.0904, n^{20}_D 1.5055, M_R 81.93; calc. 82.49.

Found %: C 59.71; H 8.75; N 4.67; S 9.80. $C_{15}H_{27}O_3NS$. Calculated %: C 59.75; H 9.03; N 4.65; S 10.62.

When the compound obtained was treated with methyl iodide, a solid, light yellow, very hygroscopic mass was obtained, which was readily soluble in water and chloroform; insoluble in ether. Apparently this material was a sulfonium salt.

Found %: I 29.5. $C_{16}H_{30}O_3NSI$. Calculated %: I 28.6.

SUMMARY

1. The use of the xanthogenic method for the dehydration of the ethyl ester of 3-(β -hydroxyethyl)-4-(β -carboethoxyethyl)-N-acetylpiperidine with the formation of the ethyl ester of racemic N-acetylhomomeroquinene has been described.

2. It has been established that when β -[4-(β '-carboxyethyl)piperidyl-(3)]ethyltrimethylammonium is cleaved in alkaline medium, β -[1,3-ethylenepiperidyl-(4)]propionic acid is formed. Consequently, when the quaternary base containing a labile hydrogen in the δ '-position breaks down, a five-membered ring is formed instead of the ethylene derivative.

The possibility that this reaction is of a general nature and might prove to be useful for the production of five- and six-membered rings is not excluded.

LITERATURE CITED

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SYNTHESIS OF 3-(α -DIETHYLAMINOETHYL)-4-METHYLPYRIDINE

L. N. Yakhontov and M. V. Rubtsov

S. Ordzhonikidze All-Union Scientific Research Chemicopharmaceutical Institute

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In a previous communication [1] we described the synthesis of 3-(α -diethylaminoethyl)pyridine and its conversion to 3-vinylpiperidine.

3-(α -Diethylaminoethyl)-4-methylpyridine (I) can serve as the starting material for the preparation by a similar method of 4-substituted 3-vinylpiperidines (meroquinene, homomeroquinene, etc.).

The present paper is devoted to the description of a practicable method for the synthesis of (I) and to a study of some reactions of the intermediate compounds. The conversions carried out can be represented by the diagram shown on the following page.

As the starting material we used trichlorocollidine (II) [2], which was converted to 3-(α -hydroxyethyl)-4-methylpyridine (XVIII) by three different routes.

As we have shown previously [3], when (II) is treated with an alcoholic solution of sodium hydroxide, it is converted with a 98% yield to 2,6-dichloro-3-vinyl-4-methylpyridine (III), which readily adds a molecule of bromine at the double bond to form 2,6-dichloro-3-(α,β -dibromoethyl)-4-methylpyridine (IV).

Preliminary experiments showed that the addition of hydrogen chloride at the double bond when an acetic acid solution of (III) was saturated with gaseous hydrogen chloride took place with a yield of about 13%. Carrying

* Original Russian pagination. See C.B. translation.



When (VIII) was reacted with hydrazine hydrate at room temperature, even in the case of equimolar quantities of the starting materials, the reaction product was the dihydrochloride of 3,4-(6'-hydrazino-4'-methylpyridino-2',3')pyrazolone-5 (IX). An increase in the amount of hydrazine hydrate introduced into the reaction made it possible to raise the yield of (IX) to 93.5%. This reaction apparently can also be used for the synthesis of other derivatives of the condensed pyridinopyrazolone system.

Dehalogenation of 2,6-dichloro-4-methylnicotinic acid both with Raney nickel as a catalyst under pressure, and in the presence of palladium, led to 4-methylnicotinic acid (X), identical with (X) prepared from lepidine through 4-methylquinolinic acid [6]. The ethyl ester of 4-methylnicotinic acid (XI) was converted by a method mentioned in the literature [6] to 3-acetyl-4-methylpyridine (XII). In accordance with the literature data [7], the condensation of ethyl acetate with (XI) proceeded less smoothly than with other esters of the pyridinecarboxylic acids. The yield of 3-acetyl-4-methylpyridine did not exceed 35%. In the presence of platinum catalyst (XII) was reduced to 3-(α -hydroxyethyl)-4-methylpyridine (XVIII) [4,8].

The total yield of (XVIII) when synthesized by the first route from trichlorocollidine through 2,6-dichloro-3-vinyl-4-methylpyridine (III), 2,6-dichloro-4-methylnicotinic acid (VII), 4-methylnicotinic acid (X), its ethyl ester, and 3-acetyl-4-methylpyridine (XII) was 13%, based on the trichlorocollidine.

The synthesis of 3-(α -hydroxyethyl)-4-methylpyridine (XVIII) by the second route was based on the conversion of trichlorocollidine through 3-(β -chloroethyl)-4-methylpyridine (XIII) to 3-vinyl-4-methylpyridine (XIV) [2]. Compound (XIV), in contrast to the corresponding 2,6-dichloro derivative (III), when it was reacted with calcium hypochlorite formed the chlorohydrin (XV) in 76% yield. The 3-(α -hydroxy- β -chloroethyl)-4-methylpyridine (XV) obtained in this way was converted by treatment with an alcoholic solution of sodium hydroxide to 3-acetyl-4-methylpyridine which, as in the synthesis by the first route, was reduced to 3-(α -hydroxyethyl)-4-methylpyridine (XVIII). The total yield of (XVIII) based on trichlorocollidine was 10% in this case.

It proved to be much more convenient to prepare 3-(α -hydroxyethyl)-4-methylpyridine (XVIII) from trichlorocollidine (II) by the third route: through 2,6-dichloro-3-vinyl-4-methylpyridine (III), 2,6-dichloro-4-methylnicotinic acid (VII), and 2,6-dichloro-3-acetyl-4-methylpyridine (XVI). Compound (XVI) was prepared by the reaction of 2,6-dichloro-4-methylnicotinyl chloride and ethoxymagnesiummalonic ester, with subsequent hydrolysis and decarboxylation of the 2,6-dichloro-4-methyl-3-(β , β -dicarboethoxyacetyl)pyridine that was formed, by boiling it in a mixture of acetic and sulfuric acids. When (XVI) was reacted with sodium borohydride, only the keto group was reduced, but when (XVI) was hydrogenated in the presence of palladium catalyst, dehalogenation took place, as well as reduction of the keto group, and 3-(α -hydroxyethyl)-4-methylpyridine (XVIII) was formed in quantitative yield. The total yield of (XVIII) based on trichlorocollidine, by the third route was 44.3%.

Reaction of 3-(α -hydroxyethyl)-4-methylpyridine hydrochloride with thionyl chloride led to the formation of 3-(α -chloroethyl)-4-methylpyridine hydrochloride (XIX) in quantitative yield, and treatment of (XIX) with an excess of diethylamine in a sealed tube at 120° permitted preparation of 3-(α -diethylaminoethyl)-4-methylpyridine in 70.5% yield.

EXPERIMENTAL

2,6-Dichloro-4-methylnicotinic acid. To 57.9 g of 2,6-dichloro-3-vinyl-4-methylpyridine in 500 ml of acetone was added, with stirring, 129.8 g of potassium permanganate in 13 g portions, while the temperature of the reaction mixture was maintained at 25-30°. When the reaction was ended, the precipitate of manganese dioxide was filtered off and washed with acetone, then boiled twice with 150-ml portions of water. The water-acetone solution was evaporated in vacuum to a volume of 50 ml and the unreacted 2,6-dichloro-3-vinyl-4-methylpyridine (14.5 g) was extracted with ether. The aqueous solution was acidified to Congo with concentrated hydrochloric acid and extracted with ether. The extract was dried with calcined sodium sulfate. After the ether had been distilled off, 45.6 g of a thick oily material was obtained, which crystallized when triturated with toluene. By recrystallization from 80 ml of toluene, 34 g (71.5%) of 2,6-dichloro-4-methylnicotinic acid was obtained with m.p. 140-141°. Colorless crystals. The compound was readily soluble in ether, acetone, chloroform, ethyl acetate, and alcohol; poorly soluble in benzene and toluene; insoluble in water, ligroin, and petroleum ether.

Found %: C 41.12, 40.68; H 2.58, 2.62; N 6.50, 6.75; Cl 34.42. $C_7H_5O_2NCl_2$. Calculated %: C 40.78; H 2.43; N 6.79; Cl 34.47.

The compound did not form a hydrochloride, picrate, or methiodide under the usual conditions.

Ethyl ester of 2,6-dichloro-4-methylnicotinic acid. 2.5 g of 2,6-dichloro-4-methylnicotinic acid was boiled for 1 hr with 16 ml of purified thionyl chloride. The solution obtained was evaporated in vacuum and the residual thionyl chloride was removed by twice adding benzene and subsequently distilling it off in vacuum. The 2,6-dichloro-4-methylnicotinyl chloride obtained in this way was boiled with 20 ml of anhydrous alcohol for 3.5 hr. Then the solution was evaporated in vacuum and the residue was treated with 50% potassium carbonate solution and extracted with ether. The ether extract was dried with calcined sodium sulfate, the ether was distilled off, and the ethyl ester of 2,6-dichloro-4-methylnicotinic acid was distilled in vacuum. B.p. 153-154° (12 mm). Yield 2.6 g (91%).

The product was a colorless oily liquid, soluble in the usual organic solvents, insoluble in water, n_D^{20} 1.5248.

Found %: C 46.24, 46.08; H 4.05, 3.96; N 6.08, 6.28; Cl 29.91. $C_9H_9O_2NCl_2$. Calculated %: C 46.15; H 3.84; N 5.98; Cl 30.34.

3,4-(6'-Hydrazino-4'-methylpyridino-2',3')-pyrazolone-5. To a solution of 1.6 g of the ethyl ester of 2,6-dichloro-4-methylnicotinic acid in 5 ml of alcohol was added 0.2 g of hydrazine hydrate. The reaction mixture was left at room temperature for 12 hr. Crystals of 3,4-(6'-hydrazino-4'-methylpyridino-2',3')-pyrazolone-5 dihydrochloride precipitated. Weight 0.8 g, m.p. 264-265° (decomp.). Another gram of hydrazine hydrate was added to the mother liquor after removal of the crystals, and the mixture was left for 6 hr at room temperature. Another 0.8 g of crystals precipitated, m.p. 264-265° (decomp.). The total yield of 3,4-(6'-hydrazino-4'-methylpyridino-2',3')-pyrazolone-5 dihydrochloride was 1.6 g (93.5%). The product was a white crystalline material, poorly soluble in water and the usual organic solvents.

Found %: N 27.70, 27.47; Cl 27.94, 27.86. $C_7H_9ON_5 \cdot 2HCl$. Calculated %: N 27.77; Cl 28.17.

Dehalogenation of 2,6-dichloro-4-methylnicotinic acid. 1) A solution of 2 g of 2,6-dichloro-4-methylnicotinic acid in 30 ml of alcohol was hydrogenated at 18-20° and a pressure of 20-30 cm of water, in the presence of palladium catalyst prepared from 2 g of palladous chloride. The absorption of hydrogen gradually slowed down. When the reaction was ended, the catalyst was filtered off and the filtrate was evaporated in vacuum. The residue (1.75 g) was triturated with anhydrous ether and washed on the filter with anhydrous alcohol. 0.7 g of 4-methylnicotinic acid hydrochloride was obtained as colorless crystals, m.p. 140-141° (decomp.). From the ether solution after removal of the ether we obtained 1.05 g of 2,6-dichloro-4-methylnicotinic acid, m.p. 139 to 140°.

2) 2.06 g of 2,6-dichloro-4-methylnicotinic acid was dissolved in 300 ml of 0.1 N sodium hydroxide solution and hydrogenated in the presence of 2 g of Raney nickel catalyst at 50° and a pressure of 10 atm. The catalyst was filtered off; the filtrate was evaporated in vacuum to a volume of 10 ml and acidified to Congo with concentrated hydrochloric acid. Upon rubbing with a stirring rod, a white crystalline precipitate separated out, which was filtered off and washed with 1 ml of water. 0.8 g (60%) of 4-methylnicotinic acid was obtained. Colorless crystals, m.p. 218-219°. When the mother liquor was evaporated to a volume of 6 ml, another 0.6 g of 4-methylnicotinic acid precipitated, contaminated with inorganic salts, m.p. 214-215°.

3) Reduction of 2.06 g of 2,6-dichloro-4-methylnicotinic acid was carried out as in experiment 2. After the catalyst had been removed, the solution was evaporated in vacuum to dryness. To the residue were added 3 ml of concentrated sulfuric acid and 1 ml of anhydrous alcohol. The reaction mixture was boiled for 6 hr, after which it was poured onto ice, made alkaline (to phenolphthalein) with 50% potassium carbonate solution, and extracted with ether. The ether extract was dried with potassium carbonate. The ether was distilled off and the residue was distilled in vacuum. 0.9 g (54.5%) of the ethyl ester of 4-methylnicotinic acid was obtained. Colorless mobile liquid, b.p. 108-109° (8 mm), n_D^{18} 1.5070.

Picrate, yellow crystals (from alcohol), m.p. 137-138°.

2,6-Dichloro-3-acetyl-4-methylpyridine. The 2,6-dichloro-4-methylnicotinyl chloride prepared as described above from 17 g of the acid was dissolved in 50 ml of anhydrous benzene and added to ethoxymagnesium-

*In the literature the following data are given for the m.p. of 4-methylnicotinic acid: 218-219° [4]; 211-213° [9]; 215-216° [8]. For the ethyl ester of 4-nicotinic acid the values given are: b.p. 100-103° (5 mm), n_D^{18} 1.5079; picrate, m.p. 137-138° [4]; b.p. 118° (12 mm); picrate, m.p. 137° [7].

malonic ester prepared from 16 g of malonic ester.* The reaction mixture was heated for 1 hr on a boiling water bath, after which it was evaporated at a residual pressure of 5 mm and 100°. The 2,6-dichloro-4-methyl-3-(β , β -dicarboethoxyacetyl)pyridine was hydrolyzed and partially decarboxylated by boiling for 12 hr with 20 ml of glacial acetic acid and 5 ml of concentrated sulfuric acid. The reaction mixture was evaporated in vacuum. The residue was neutralized with 50% potassium carbonate solution, extracted with ether, and the extract was dried with potassium carbonate. After the solvent had been removed, the 2,6-dichloro-3-acetyl-4-methylpyridine was distilled in vacuum. B.p. 156-158° (18 mm). Yield 10.5 g (62.7%).

The product was a colorless oily material, readily soluble in the usual organic solvents, insoluble in water; n_D^{20} 1.5457.

Found %: C 47.31, 47.16; H 3.62, 3.47; N 6.67, 6.72. $C_8H_7ONCl_2$. Calculated %: C 47.06; H 3.43; N 6.86.

The compound did not form a hydrochloride, picrate, or methiodide under the usual conditions.

2,6-Dichloro-3-(α -hydroxyethyl)-4-methylpyridine. To a solution of 2.6 g of 2,6-dichloro-3-acetyl-4-methylpyridine in 10 ml of methanol was added 2.6 g of sodium borohydride over a period of 10 min at room temperature, with stirring. The reduction process proceeded with the evolution of heat and foaming of the reaction mixture. The methanol was distilled off in vacuum. The residue was treated with 20 ml of water and extracted with ether. The ether extract was dried with potassium carbonate and evaporated in vacuum. The residue distilled at 152-153° (5 mm). Yield of 2,6-dichloro-3-(α -hydroxyethyl)-4-methylpyridine 2.5 g (96%). When the compound was triturated with petroleum ether, it completely crystallized. Colorless crystals, insoluble in water and petroleum ether; readily soluble in ether, acetone, alcohol, chloroform, and benzene; m.p. 95-96°.

Found %: C 46.43, 46.25; H 4.58, 4.63; N 6.70, 7.05; Cl 34.71, 34.66; OH 8.42, 8.10. $C_8H_9ONCl_2$. Calculated %: C 46.60; H 4.37; N 6.79; Cl 34.46; OH 8.25.

The compound did not form a hydrochloride, picrate, or methiodide under the usual conditions.

Reaction of 2,6-dichloro-3-vinyl-4-methylpyridine with hydrogen chloride. 1) A solution of 4.9 g of 2,6-dichloro-3-vinyl-4-methylpyridine in 30 ml of glacial acetic acid was saturated for 10 hr at 18-20° with dry hydrogen chloride. The reaction mixture was left for 24 hr, after which it was poured into 150 ml of water. The mixture was extracted with chloroform. The chloroform extract was washed with 25% potassium carbonate solution and dried with calcined potassium carbonate. The chloroform was distilled off. The residue was fractionally distilled in vacuum. The fractions collected were as follows: 1st fraction, b.p. 142-143° (16 mm), weight 3.7 g. The material gave a positive reaction for a double bond with potassium permanganate and was the starting material, 2,6-dichloro-3-vinyl-4-methylpyridine. 2nd fraction, b.p. 149° (5 mm), weight 0.75 g (12.8%). The material crystallized; m.p. 69°. The compound obtained was trichlorocollidine. When a mixed sample 2,6-dichloro-3-(β -chloroethyl)-4-methylpyridine (trichlorocollidine) was melted, no depression in melting point was observed.

2) 3.7 g of 2,6-dichloro-3-vinyl-4-methylpyridine was dissolved in 25 ml of glacial acetic acid saturated with hydrogen chloride. The reaction mixture was heated in a sealed tube at 140° for 6 hr. The treatment was as in experiment 1. 2.2 g of 2,6-dichloro-3-vinyl-4-methylpyridine and 1.4 g (32%) of trichlorocollidine with m.p. 69° were obtained.

2,6-Dichloro-3-(β -bromovinyl)-4-methylpyridine. To 18.7 g of 2,6-dichloro-3-(α , β -dibromomethyl)-4-methylpyridine in 20 ml of anhydrous alcohol was added a solution of 2.5 g of sodium hydroxide in 60 ml of anhydrous alcohol. The reaction mixture spontaneously heated up and a precipitate of sodium bromide separated out, mixed with 2,6-dichloro-3-(β -bromovinyl)-4-methylpyridine, which is poorly soluble in cold alcohol. After standing for 30 min at 18-20°, the reaction mixture was heated to boiling and the sodium bromide was filtered off. The alcoholic filtrate was evaporated in vacuum. The 2,6-dichloro-3-(β -bromovinyl)-4-methylpyridine was distilled, b.p. 158-160° (27 mm). Yield 12.7 g (97%). When rubbed with a stirring rod, the compound crystallized.

* The ethoxymagnesiummalonic ester was prepared in the following way: 3.6 g of magnesium turnings, activated with iodine and 3 drops of carbon tetrachloride, were heated with 50 ml of anhydrous alcohol at 90-100° until the magnesium was completely converted to magnesium ethylate. Then 16 g of malonic ester was added and heated for 1 hr at 100°. The excess alcohol was distilled off at 50° (10 mm).

The product formed colorless crystals, m.p. 109-110°, readily soluble in ether, acetone, benzene, toluene, and chloroform; poorly soluble in alcohols; insoluble in water.

Found %: C 36.33; H 2.43; N 5.20; Cl 26.09; Br 29.63. $C_8H_6NCl_2Br$. Calculated %: C 35.95; H 2.25; N 5.24; Cl 26.59; Br 29.96.

The compound gave a positive reaction for a double bond (with $KMnO_4$), and did not form a hydrochloride, picrate, or methiodide under the usual conditions.

2,6-Dichloro-3-(β -chlorovinyl)-4-methylpyridine. 1) To a mixture of 28.2 g of 2,6-dichloro-3-vinyl-4-methylpyridine and 70 ml of water, vigorously stirred in an atmosphere of carbon dioxide gas, was added over a period of 1 hr at room temperature 220 ml of an aqueous solution of calcium hypochlorite containing 9.24 g of active chlorine. The reaction mixture was stirred for 1 hr more at 18-20°, acidified to Congo with nitric acid, and extracted with ether. The ether was distilled off and the residue was distilled in vacuum. The fraction boiling at 171-190° (13 mm) was collected. 23.45 g of 2,6-dichloro-3-(α,β -dichloroethyl)-4-methylpyridine and the corresponding chlorohydrin were obtained, including about 4% of the latter (determined from the labile hydrogen content).

17.3 g of the mixture obtained with b.p. 171-190° (13 mm) was dissolved in 10 ml of anhydrous alcohol and treated at room temperature with 5.4 g of sodium hydroxide in 20 ml of anhydrous alcohol. When this was done, heat was evolved and sodium chloride precipitated. After standing for 30 min at 18-20°, the sodium chloride was filtered off and the alcohol was distilled off in vacuum. The residue was recrystallized from methanol. Yield of 2,6-dichloro-3-(β -chlorovinyl)-4-methylpyridine 14.71 g (41.58%, calculated on the basis of 2,6-dichloro-3-vinyl-4-methylpyridine). Colorless crystals, m.p. 88-89°, b.p. 149-150° (7 mm). The compound was readily soluble in ether, acetone, chloroform, and benzene; less soluble in alcohols; insoluble in water.

Found %: C 43.28, 43.02; H 2.79, 2.52; N 6.30; Cl 47.77, 47.97. $C_8H_6NCl_3$. Calculated %: C 43.16; H 2.69; N 6.29; Cl 47.84.

2) 28.8 g of 2,6-dichloro-3-vinyl-4-methylpyridine was treated with 133 ml of an aqueous solution of calcium hypochlorite containing 5.6 g of active chlorine, under the conditions described in experiment 1. After acidification of the reaction mixture with nitric acid and extraction with ether, we obtained 34.7 g of a mixture of products, which was treated, without preliminary fractionation in vacuum, with 10.4 g of sodium hydroxide in 60 ml of anhydrous alcohol. After standing at room temperature for 30 min, the sodium chloride that had precipitated during the reaction was filtered off. The alcoholic filtrate was evaporated in vacuum. The residue was distilled. The following fractions were collected: 1st fraction, b.p. 142-143° (16 mm), weight 10.45 g (36.3%), was the starting 2,6-dichloro-3-vinyl-4-methylpyridine; 2nd fraction, b.p. 149-150° (7 mm), weight 7.02 g (18%), crystallized when triturated with alcohol. M.p. 88-89°. A mixed sample with 2,6-dichloro-3-(β -chlorovinyl)-4-methylpyridine obtained in experiment 1 gave no depression in melting point.

Hydrogenation of 2,6-dichloro-3-(β -chlorovinyl)-4-methylpyridine. 3 g of 2,6-dichloro-3-(β -chlorovinyl)-4-methylpyridine in 80 ml of dioxane was hydrogenated in the presence of 1 g of Raney nickel catalyst at room temperature, and a pressure of 25-30 cm of water. After 1 mole (0.3 liter) of hydrogen had been absorbed, the hydrogenation was discontinued. The catalyst was filtered off, the filtrate was evaporated in vacuum, and the residue was distilled. B.p. 159-161° (10 mm).* Yield 2.95 g (98%). The compound crystallized, m.p. 69-70°.* A mixed sample with trichlorocollidine gave no depression in melting point.

3-(α -Hydroxy- β -chloroethyl)-4-methylpyridine. To a solution of 4.5 g of 3-vinyl-4-methylpyridine in 30 ml of water was added, at room temperature with vigorous stirring in an atmosphere of carbon dioxide gas, drop by drop over a period of 10 min, 26 ml of an aqueous solution of calcium hypochlorite containing 1.06 g of active chlorine. A few minutes after the reaction started, the solution became turbid and an oily precipitate began to separate out. After the mixture had been stirred for 2 hr at 18-20°, the precipitate crystallized. The reaction mixture was treated with 50% potassium carbonate solution and extracted with chloroform. The dried chloroform solution was treated with an alcoholic solution of hydrogen chloride until there was an acid reaction

*In the literature the following data are given: m.p. 69-70°, b.p. 160-161° (10 mm) [2].

to Congo, and then was evaporated to dryness. The residue was recrystallized from anhydrous alcohol. 4.8 g (76%) or 3-(α -hydroxy- β -chloroethyl)-4-methylpyridine hydrochloride was obtained. Colorless crystals, m.p. 153-154°. The compound was readily soluble in water, poorly soluble in acetone and alcohol, insoluble in ether.

Found %: C 46.27, 46.59; H 5.55, 5.25; N 6.50, 6.62; Cl 33.82. $C_8H_{10}ONCl \cdot HCl$. Calculated %: C 46.16; H 5.29; N 6.73; Cl 34.13.

3-Acetyl-4-methylpyridine. 4.2 g of 3-(α -hydroxy- β -chloroethyl)-4-methylpyridine was boiled for 5 min with 2.1 g of sodium hydroxide in 40 ml of anhydrous alcohol. The sodium chloride that precipitated was filtered off. The alcoholic filtrate was evaporated in vacuum. The residue was treated with 16% sodium carbonate solution and extracted with ether. The ether extract was evaporated in vacuum and fractionally distilled. A fraction boiling at 100-102° (8 mm)* was collected. Yield of 3-acetyl-4-methylpyridine 0.75 g (31%). Colorless oily material, soluble in the usual organic solvents and in water; n_D^{20} 1.5326.

The compound gave a negative Beilstein test for chlorine and was identical with 3-acetyl-4-methylpyridine synthesized as described in the literature [7] from the ethyl ester of 4-methylnicotinic acid in 35% yield.**

Picrate, yellow crystals, m.p. 145-147°.

Found %: N 15.40. $C_8H_9ON \cdot C_6H_3O_7N_3$. Calculated %: N 15.38.

3-(α -Hydroxyethyl)-4-methylpyridine. 1). A solution of 3.3 g of 3-acetyl-4-methylpyridine in 60 ml of distilled water was hydrogenated at 18-20° and a pressure of 25-30 cm of water, in the presence of platinum catalyst prepared as described by Adams. The catalyst was filtered off and the filtrate was treated with 5 ml of concentrated hydrochloric acid and evaporated in vacuum. The crystalline residue was washed with anhydrous acetone. 3.9 g (95%) of 3-(α -hydroxyethyl)-4-methylpyridine hydrochloride was obtained. Colorless crystals, m.p. 154-155°. The compound was readily soluble in water and alcohols; insoluble in ether, acetone, benzene, and chloroform.

Found %: Cl 20.37. $C_8H_{11}ON \cdot HCl$. Calculated %: Cl 20.46.

The base was an oily, colorless compound with an aromatic odor, b.p. 140-142° (3 mm).***

2) A solution of 9.4 g of 2,6-dichloro-3-acetyl-4-methylpyridine in 70 ml of alcohol was hydrogenated at 18-20° and a pressure of 25-30 cm of water, in the presence of palladium catalyst prepared from 4.8 g of palladium chloride. The reaction mixture was treated as described above. Yield of 3-(α -hydroxyethyl)-4-methylpyridine hydrochloride 7.99 g (100%), m.p. 154-155°. The compound gave no depression in melting point when mixed with 3-(α -hydroxyethyl)-4-methylpyridine prepared by the reduction of 3-acetyl-4-methylpyridine.

3) 2.6 g of 2,6-dichloro-3-(α -hydroxyethyl)-4-methylpyridine was hydrogenated in 20 ml of alcohol at 18-20° and a pressure of 25-30 cm of water, in the presence of palladium catalyst prepared from 2 g of palladium chloride. Yield of 3-(α -hydroxyethyl)-4-methylpyridine hydrochloride 2.17 g (100%), m.p. 154-155°.

3-(α -Chloroethyl)-4-methylpyridine. To a mixture of 1.7 g of 3-(α -hydroxyethyl)-4-methylpyridine hydrochloride in 20 ml of anhydrous benzene was added 2.3 g of thionyl chloride. The reaction mixture was left at 18-20° for 12 hr, then heated for 2 hr at 60° and evaporated in vacuum. Yield of 3-(α -chloroethyl)-4-methylpyridine hydrochloride 1.92 g (100%). Colorless crystals, m.p. 162-162.5° (from acetone). The compound was soluble in water, alcohols, and chloroform; poorly soluble in acetone; insoluble in ether and benzene.

Found %: C 50.28; H 5.91; N 7.15; Cl 37.28. $C_8H_{10}NCl \cdot HCl$. Found %: C 50.00; H 5.72; N 7.29; Cl 36.98.

3-(α -Diethylaminoethyl)-4-methylpyridine. A mixture of 1.7 g of 3-(α -chloroethyl)methylpyridine hydrochloride and 20 g of diethylamine was heated for 10 hr in a sealed tube at 120°. The contents of the tube were treated with 50% potassium carbonate solution and extracted with ether. The ether solution was dried with

*In the literature the following data are given for 3-acetyl-4-methylpyridine: b.p. 100-102° (8 mm), picrate m.p. 145-147° [4]. See also [7,8].

**In the literature [7], yields of 35.8 and 23.4% are reported.

***In the literature the following data are given for 3-(α -hydroxyethyl)-4-methylpyridine: b.p. 139-143° (3 mm) [4]; b.p. 108-110° (1.2 mm), hydrochloride, m.p. 148-149° [8].

calcined potassium carbonate and evaporated in vacuum. The residue was distilled at 104° (4 mm). Yield of 3-(α -diethylaminoethyl)-4-methylpyridine 1.2 g (70.5%). Light yellow oily compound, quickly turning dark in the air. Readily soluble in the usual organic solvents, less soluble in water, n_D^{20} 1.5067.

Found %: C 75.12; H 10.36; N 14.45. $C_{12}H_{20}N_2$. Calculated %: C 75.00; H 10.42; N 14.58.

Dipicrate, yellow crystals, m.p. 202-203° (from alcohol).

Found %: N 17.33. $C_{12}H_{20}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: N 17.23.

SUMMARY

1. Three schemes for the synthesis of 3-(α -hydroxyethyl)-4-methylpyridine from trichlorocollidine have been studied: a) through 3-(β -chloroethyl)-4-methylpyridine, 3-vinyl-4-methylpyridine, 3-(α -hydroxy- β -chloroethyl)-4-methylpyridine, and 3-acetyl-4-methylpyridine, with a total yield of 10%; b) through 2,6-dichloro-3-vinyl-4-methylpyridine, 2,6-dichloro-4-methylnicotinic acid, 4-methylnicotinic acid; its ethyl ester, and 3-acetyl-4-methylpyridine, with a total yield of 13%; c) through 2,6-dichloro-3-vinyl-4-methylpyridine, 2,6-dichloro-4-methylnicotinic acid, and 2,6-dichloro-3-acetyl-4-methylpyridine, with a total yield of 44.3%.

2. The synthesis of 3-(α -diethylaminoethyl)-4-methylpyridine has been carried out, starting from trichlorocollidine, in six stages with a total yield of 31.2%.

3. The preparation of a derivative of 3,4-(pyridino-2',3')pyrazolone-5 by the reaction of the ethyl ester of a substituted 2-chloronicotinic acid with hydrazine hydrate has been described.

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INVESTIGATIONS IN THE PHENOXAZINE SERIES

1. SYNTHESIS OF SOME 10-SUBSTITUTED PHENOXAZINES

V. G. Samolovova, T. V. Gortinskaya, and M. N. Shchukina

S. Ordzhonikidze All-Union Research Institute of Chemical Pharmaceutics

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N-Dialkylaminoalkyl derivatives of phenothiazine and a series of their analogs possess high pharmacological activity [1]. Interest is therefore attached to the preparation of analogous compounds of the phenoxazine

*Original Russian pagination. See C.B. translation.

series. Only a small number of 10-substituted phenoxazines have so far been described: methyl, ethyl, phenyl, benzyl, acetyl, and a few others [2].

These compounds were prepared mainly by cyclization of N-alkyl- or N-aryldiphenylamines. N-Alkyl-substituted phenoxazines were first synthesized [3] by reaction of alkyl halides with 10-Na-phenoxazine. The latter was obtained by reaction of phenoxazine with sodium amide.

10-Arylphenoxazines were prepared by heating phenoxazine with aryl iodides in presence of potassium carbonate and copper bronze. 10-(3-Diethylaminoethyl)-phenoxazine has also been prepared [4] by heating phenoxazine with diethylaminoethyl chloride and solid sodium hydroxide.

With the objective of preparing 10-(3-dimethylaminopropyl)-phenoxazine, which is of interest as an analog of 10-(dimethylaminopropyl)-phenothiazine, we carried out the condensation of phenoxazine with acrylonitrile and hydrogenated the resulting 10-(2-cyanoethyl)-phenoxazine in presence of skeletal nickel catalyst to obtain 10-(3-aminopropyl)-phenoxazine. We tried to methylate the latter with formalin and formic acid, but obtained a substance insoluble in organic solvents and defying our attempts at purification and elucidation of its structure. Heating of 10-(2-cyanoethyl)-phenoxazine with concentrated sulfuric acid at 50° gave 2-(10-phenoxazyl)-propionamide, and boiling of the latter with a mixture of methanol and concentrated hydrochloric acid converted it into 2-(10-phenoxazyl)-propionic acid. We prepared 10-(3-dimethylaminopropyl)-phenoxazine by heating phenoxazine and 3-dimethylaminopropyl chloride with solid sodium hydroxide.

EXPERIMENTAL

10-(2-Cyanoethyl)-phenoxazine. In the course of 30 min, 54.2 ml of acrylonitrile was stirred into a suspension of 25 g of phenoxazine and 1.5 ml of Rodionov catalyst (trimethylphenylammonium hydroxide) in 50 ml of anhydrous benzene. The mixture was boiled for an hour and stood until the next day. The precipitate was filtered and washed with warm water. There was obtained 25.85 g (77%) of faint-yellow crystals, soluble in alcohol; m.p. 123-124° (from alcohol).

Found %: C 75.60; H 5.38. $C_{15}H_{12}ON_2$. Calculated %: C 76.25; H 5.14.

10-(3-Aminopropyl)-phenoxazine. A mixture of 25 g of 10-(2-cyanoethyl)-phenoxazine and 250 ml of 15% alcoholic ammonia was treated with hydrogen at 50° and 50 atm in presence of 10 g of nickel catalyst paste. After hydrogen ceased to be absorbed, the catalyst was filtered off, the filtrate evaporated to dryness in vacuo, and the residue distilled at 1 mm and 194-200° to give 19.4 g (76.6%) of 10-(3-aminopropyl)-phenoxazine. Colorless crystals with m.p. 63-64°, soluble in alcohol.

Found %: C 74.47; H 6.68; N 11.27. $C_{15}H_{14}ON_2$. Calculated %: C 75.01; H 6.71; N 11.66.

2-(10-Phenoxazyl)-propionamide. A mixture of 6.9 g of 10-(2-cyanoethyl)-phenoxazine and 22 ml of conc. H_2SO_4 was heated at 50° for 1.5 hr, then cooled and poured onto ice. The precipitate was filtered, washed with water, and dried. Recrystallization from alcohol gave 5.45 g of slightly pinkish crystals with m.p. 173-174°.

Found %: N 11.01. $C_{15}H_{14}O_2N_2$. Calculated %: N 11.03.

2-(10-Phenoxazyl)-propionic acid. 2-(10-Phenoxazyl)-propionamide (0.66 g) was boiled for 1.5 hr with a mixture of 7.5 ml of methanol and 1 ml of concentrated hydrochloric acid. After the reaction mass had cooled, 1 ml of 40% sodium hydroxide was added and boiling continued for 1.5 hr. The precipitate was filtered and the filtrate acidified with 20% hydrochloric acid. There was obtained 0.55 g of colorless crystals, m.p. 138-139° (from methanol).

Found %: C 70.49; H 5.26; N 5.59. $C_{15}H_{13}O_3N$. Calculated %: C 70.60; H 5.13; N 5.49.

10-(3-Dimethylaminopropyl)-phenoxazine. A mixture of 15.8 g of phenoxazine, 26 g of 3-dimethylaminopropyl chloride, and 6.9 g of solid sodium hydroxide was heated for 13 hr at 100°. After cooling, the mixture was extracted with ether, the ethereal extract was washed with 150 ml of water and extracted 4 times with 20-ml portions of 10% phosphoric acid. To the phosphoric acid solution was added 160 ml of water, followed by 40% alkali solution, until the liquid was alkaline to phenolphthalein. The alkaline solution was extracted with ether and dried with calcined sodium sulfate. The ether was driven off and the residue distilled at 0.8-1 mm and 184-187°. The product was soluble in anhydrous ethyl acetate, and the 10-(3-dimethylaminopropyl)-phenoxazine hydrochloride was isolated by addition of alcoholic hydrogen chloride until the mass was acid to Congo. It was recrystallized from absolute alcohol. Yield 6.82 g of hydrochloride, melting at 100-104° with decomp.

Found %: C 66.82; H 6.77; N 11.65. $C_{17}H_{21}ON_2Cl$. C 67.16; H 6.94; N 11.63.

SUMMARY

1. Cyanoethylation of phenoxazine gave 10-(2-cyanoethyl)-phenoxazine, which was reduced to 10-(3-aminopropyl)-phenoxazine. Hydrolysis of the latter gave 2-(10-phenoxazyl)-propionamide and 2-(10-phenoxazyl)-propionic acid.

2. Heating of phenoxazine with 3-dimethylaminopropyl chloride in presence of solid sodium hydroxide gave 10-(3-dimethylaminopropyl)-phenoxazine, which was converted to the hydrochloride.

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SOME PYRIDAZINE DERIVATIVES

T. V. Gortinskaya and M. N. Shchukina

S. Ordzhonikidze All-Union Research Institute of Chemical Pharmaceutics

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Hydrazino derivatives of phthalazine, notably 1-hydrazinophthalazine [1] (Apresoline) and 1,4-dihydrazinophthalazine [2] (Nepresol), possess considerable hypotensive activity. It was therefore of interest to prepare analogous pyridazine derivatives.

We prepared 3,6-dihydrazinopyridazine [3] from 3,6-dichloropyridazine in good yield by the literature method [4].

3,6-Dihydrazinopyridazine could not be prepared directly from 3,6-dichloropyridazine by the action of hydrazine hydrate, since only 3-chloro-6-hydrazinopyridazine is formed in an alcoholic medium, while in the absence of a solvent a difficultly separable mixture is formed, comprising hydrochlorides of hydrazine and apparently 3,6-dihydrazinopyridazine. The excess of hydrazine could not be eliminated after conversion of the reaction products to the free bases, since the attempt led to resinification. Formation of a mixture of hydrochlorides was avoided by converting 3,6-dichloropyridazine into 3,6-dimethoxypyridazine [3], which was then heated with hydrazine hydrate to give 3,6-dihydrazinopyridazine. The latter was isolated and purified in the form of its dihydrochloride (m.p. 221-222°) and monohydrochloride (m.p. 232-233°).

Pharmacological investigation* of 3,6-dihydrazinopyridazine showed the preparation to be lacking in pharmacological activity of any interest.

Condensation of 3,6-dihydrazinopyridazine with aromatic aldehydes gave a series of monosubstituted hydrazones; disubstituted hydrazones could not be prepared.

*In the department of pharmacology of our institute.

2-Butoxy-5-aminopyridine is known to possess high tuberculostatic activity [5]. 3-Butoxy-6-aminopyridazine and its acetyl derivative were therefore prepared. However, they were found to possess only feeble tuberculostatic activity (at a dilution of 1:4000 to 1:1000).

3,6-Diaminopyridazine and 3-chloro-6-nitroaminopyridazine were likewise prepared; reduction of the latter did not lead to the expected 3-chloro-6-hydrazinopyridazine but to the original 3-chloro-6-aminopyridazine.

EXPERIMENTAL

3,6-Dihydrazinopyridazine hydrochloride. To a boiling solution of 5 g of 3,6-dimethoxypyridazine in 15 ml of hydrazine hydrate was gradually added (over a period of 5 hr) another 20 ml of hydrazine hydrate. Crystals of 3,6-dihydrazinopyridazine came down on the following day and were filtered, washed with alcohol, and dried. There was obtained 1 g of substance with m.p. about 220°, which decomposed when attempts were made to recrystallize it from organic solvents. Recrystallization from 1 N hydrochloric acid gave 3,6-dihydrazinopyridazine monohydrochloride with m.p. 232-233°.

Found %: C 25.69; H 5.38; Cl 19.82; H₂O 4.74. C₄H₆N₆Cl · 0.5 H₂O. Calculated %: C 25.80; H 5.39; Cl 19.20; H₂O 4.86.

Recrystallization from concentrated hydrochloric acid gave the dihydrochloride of 3,6-dihydrazinopyridazine with m.p. 221-222°.

Found %: C 22.31; H 4.60. C₄H₁₀N₆Cl₂. Calculated %: C 22.60; H 4.70.

The filtrate remaining after separation of dihydrazinopyridazine base was evaporated to dryness; the residue was heated with concentrated hydrochloric acid until it went into solution; the solution was treated with carbon, filtered, and cooled. The deposited crystals were converted into the monohydrochloride by recrystallization from dilute hydrochloric acid.

3-(4-Acetaminobenzylidenehydrazino)-6-hydrazinopyridazine. To a hot solution of 0.7 g of 3,6-dihydrazinopyridazine in 20 ml of water was added a hot solution of 1.8 g of p-acetaminobenzaldehyde. After boiling for 45 min, the yellow precipitate was filtered off, washed with hot water, and dried. Yield 1.7 g of hydrazone. Decomp. temp. 280-281° (from glacial acetic acid).

Found %: C 55.06; H 4.98. C₁₃H₁₅ON₇. Calculated %: C 54.74; H 5.26.

The following substances were similarly prepared: 3-(4-hydroxy-3-methoxybenzylidenehydrazino)-6-hydrazinopyridazine; decomp. temp. 244-245° (from alcohol).

Found %: C 53.01; H 5.10. C₁₂H₁₄O₂N₆. Calculated %: C 52.55; H 5.11.

3-(4-Hydroxybenzylidenehydrazino)-6-hydrazinopyridazine, decomp. temp. 259-260° (from alcohol).

Found %: C 53.11; H 5.03. C₁₁H₁₂ON₆. Calculated %: C 54.08; H 4.94.

3-(4-Dimethylaminobenzylidenehydrazino)-6-hydrazinopyridazine, decomp. temp. 263-265° (from 50% acetic acid).

Found %: C 58.38; H 5.82. C₁₃H₁₇N₇. Calculated %: C 57.56; H 6.26.

3-Amino-6-butoxypyrimidine. A mixture of 5 g of 3-chloro-6-aminopyridazine and sodium butoxide (prepared from 0.9 g of sodium and 35 ml of anhydrous 1-butanol) was heated for 6 hr at 150-160°. After cooling, the precipitated sodium chloride was filtered off; the filtrate was evaporated to dryness, taken up with ethyl acetate, and dried with anhydrous sodium sulfate. The solvent was driven off and the residue distilled at 178 to 180° (8 mm) to give 4 g of 3-butoxy-6-aminopyridazine in the form of a light-orange, viscous liquid. Treatment with concentrated hydrochloric acid gave the hydrochloride with m.p. 164-165° (from a mixture of ethyl acetate and alcohol).

Found %: N 20.26; Cl 17.34. C₈H₁₄ON₃Cl. Calculated %: N 20.63; Cl 17.40.

3-Acetamino-6-butoxypyridazine. A mixture of 2 g of 3-butoxy-6-aminopyridazine and 10 ml of acetic anhydride was heated on a boiling water bath until the white precipitate went into solution. Crystals came down

on cooling and were filtered and recrystallized from alcohol (with carbon). There was obtained 1.13 g of substance with m.p. 132-132.5°.

Found %: C 57.57; H 7.18; N 19.86. $C_{10}H_{15}O_2N_3$. Calculated %: C 57.39; H 7.22; N 20.08.

3,6-Diaminopyrazine. A mixture of 5 g of 3-chloro-6-aminopyridazine, 0.15 g of copper bronze, 0.25 g of copper sulfate, and 35 ml of 35% aqueous ammonia was heated in an autoclave for 6 hr at 150-160°. The precipitate was filtered from the cooled mass and extracted with 30 ml of hot alcohol. The cooled alcoholic solution deposited 0.7 g of 3,6-diaminopyridazine with m.p. 235°.

Found %: C 43.97; H 5.56. $C_4H_6N_4$. Calculated %: C 43.64; H 5.45.

3-Chloro-6-nitraminopyridazine. Into a solution of 2 g of 3-chloro-6-aminopyridazine in 10 ml of conc. H_2SO_4 (d 1.835) at 2-3° was stirred (dropwise) 1.2 ml of HNO_3 (d 1.4). The transparent solution was poured onto ice. The resulting precipitate was filtered off, washed with iced water, and recrystallized first from water and then from alcohol. Yield 1.5 g of 3-chloro-6-nitraminopyridazine with m.p. 135°.

Found %: C 27.56; H 1.80; N 20.29. $C_4H_5O_2N_4Cl$. Calculated %: C 27.50; H 1.72; N 20.40.

The 3-chloro-6-aminopyridazine was recovered after hydrogenation of 3-chloro-6-nitraminopyridazine in presence of nickel catalyst in alcohol solution.

SUMMARY

1. The following compounds were synthesized: mono- and dihydrochlorides of 3,6-dihydrazinopyridazine; monosubstituted hydrazones with 4-acetamino-, 4-hydroxy-, 3-methoxy-, 4-hydroxy-, and 4-dimethylamino-benzaldehydes.

2. 3-Amino-6-butoxypyridazine and its acetyl derivative were prepared.

3. 3,6-Diaminopyridazine and 3-chloro-6-nitraminopyridazine were prepared.

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CONDENSATION OF o-DIAMINO DERIVATIVES OF 2-METHYLBENZOTHAZOLE WITH CARBOXYLIC ACIDS

II. THIAZOLOBENZIMIDAZOLES

S. G. Fridman

Institute of Organic Chemistry, Academy of Sciences of the UkrSSR

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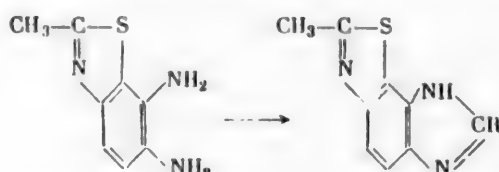
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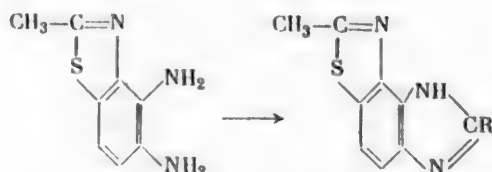
In the previous paper an account was given of the condensation of isomeric o-diamino derivatives of 2-methylbenzothiazole with α -dicarbonyl compounds, which led to three series of derivatives of thiazoloquinoxalines: thiazolo(4,5-h)quinoxalines, thiazolo(5,4-h)quinoxalines, and thiazolo(4,5-g)quinoxalines [1].

The objective of the present work was the condensation of isomeric o-diamino derivatives of 2-methylbenzothiazole with carboxylic acids. This condensation led to all of the theoretically possible isomers of thiazolobenzimidazole with a common carbon-carbon bond. They had not previously been known.

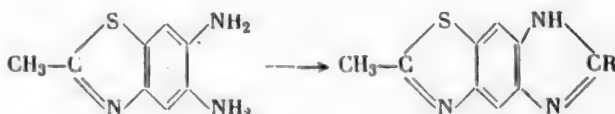
Condensation of 2-methyl-6,7-diaminobenzothiazole with carboxylic acids gives derivatives of angular thiazolo(4,5-g)benzimidazole



Condensation of 2-methyl-4,5-diaminobenzothiazole with carboxylic acids gave derivatives of the other angular isomer - thiazolo-(5,4-g)benzimidazole



Finally, condensation of 2-methyl-5,6-diaminobenzothiazole with carboxylic acids gave derivatives of the linear isomer - thiazolo(4,5-f)benzimidazole



The character of the products of condensation of aromatic o-diamines with dicarboxylic acids is known to depend on the acids used, and on the ratio of reactants. Oxalic acid and o-phenylenediamine give 2,3-dihydroxyquinoxalines, malonic acid gives o-phenylenemalonamide, and succinic acid (equimolar ratio) gives benzimidazole-2-propionic acid, while with two moles of o-phenylenediamine the product is bis-benzimidazole [2].

Condensation of o-diamino derivatives of 2-methylbenzothiazole with oxalic acid gave 2,3-dihydroxy-3-methylthiazoloquinoxalines [1], while condensation with succinic acid gave us the isomeric thiazolobenzimidazolepropionic acids. Carboxylic acids brought into reaction were formic, acetic, propionic, glycolic, lactic, benzoic, phenylacetic, and succinic. Condensation was also effected with urea and carbon disulfide.

TABLE 1

Prep. No.	R	Yield (%)	Melting point	Empirical formula	% N		% S	
					found	calc.	found	calc.

Thiazolo(4,5-g)benzimidazoles

I	H	74	213°	C ₉ H ₇ N ₃ S	21.99, 21.98	22.22	16.82, 16.91	16.93
II	CH ₃	90	204	C ₁₀ H ₉ N ₃ S	20.37, 20.39	20.69	16.08, 16.10	15.76
III	C ₆ H ₅	65	210—213	C ₁₁ H ₁₁ N ₃ S	18.95, 18.97	19.35	14.50, 14.49	14.74
IV	CH ₂ OH	74	230	C ₁₀ H ₉ O ₃ N ₃ S	18.98, 19.00	19.17		
V	CH—CH ₃ OH	58	140 (dec.)	C ₁₁ H ₁₁ ON ₃ S	17.78, 17.83	18.02	13.70, 13.60	13.73
VI	C ₆ H ₅	35	139 (dec)	C ₁₅ H ₁₁ N ₃ S	15.95, 15.94	15.84	12.06, 12.36	12.07
VII	CH ₂ C ₆ H ₅	38	263—264	C ₁₆ H ₁₃ N ₃ S	14.98, 14.93	15.05	11.53, 11.55	11.46
VIII	CH ₂ CH ₂ COOH	16	244—245	C ₁₂ H ₁₁ O ₃ N ₃ S	15.83	16.09	11.96	12.29
IX	OH	77	>330	C ₉ H ₇ ON ₃ S			15.68, 15.43	15.60
X	SH	63	>330	C ₈ H ₇ N ₃ S ₂			29.20, 29.12	28.95

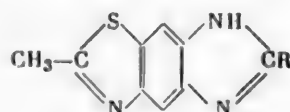
Thiazolo(5,4-g)benzimidazoles

XI	H	80	297—298	C ₉ H ₇ N ₃ S			16.97, 16.93	16.93
XII	CH ₃	68	242	C ₁₀ H ₉ N ₃ S			15.86, 15.74	15.76
XIII	C ₂ H ₅	76	194	C ₁₁ H ₁₁ N ₃ S	19.29, 19.42	19.35	14.90, 14.88	14.74
XIV	CH ₂ OH	54	245—246	C ₁₀ H ₉ ON ₃ S	18.87, 18.89	19.17	14.58, 14.57	14.56
XV	CH—CH ₃ OH	37	222	C ₁₁ H ₁₁ ON ₃ S			13.75, 13.81	13.73
XVI	C ₆ H ₅	47	118—119	C ₁₅ H ₁₁ N ₃ S	15.87, 15.77	15.84	11.37, 11.17	12.07
XVII	CH ₂ C ₆ H ₅	37	244—245	C ₁₆ H ₁₃ N ₃ S	14.80, 14.78	15.05	11.57, 11.53	11.46

TABLE 1 (continued)

Prep. No.	R	Yield (%)	Melting point	Empirical formula	% N		% S	
					found	calc.	found	calc.
XVIII	CH ₂ CH ₂ COOH	12	251—252	C ₁₂ H ₁₁ O ₂ N ₃ S			12.38, 12.24	12.29
XIX	OH	53	>325	C ₉ H ₇ ON ₃ S			15.42, 15.31	15.60
XX	SH	57	>325	C ₉ H ₇ N ₃ S ₂			28.62, 28.74	28.95

Thiazolo(4,5-f)benzimidazoles



XXI	H	61	283	C ₉ H ₇ N ₃ S • 2H ₂ O	18.62, 18.55	18.66	14.17, 14.23	14.22
XXII	CH ₃	58	244	C ₁₀ H ₉ N ₃ S • H ₂ O	18.92, 18.77	19.00	14.60, 14.69	14.48
XXIII	C ₂ H ₅	71	215—216	C ₁₁ H ₁₁ N ₃ S			14.55, 14.47	14.74
XXIV	CH ₂ OH	65	234—235	C ₁₀ H ₉ ON ₃ S	18.91, 18.82	19.17	14.72, 14.76	14.56
XXV	CHCH ₃ OH	60	127 (dec.)	C ₁₁ H ₁₁ ON ₃ S			13.35, 13.34	13.73
XXVI	C ₆ H ₅	35	254—255	C ₁₅ H ₁₃ N ₃ S	15.67, 15.65	15.84	12.03, 12.12	12.07
XXVII	CH ₂ C ₆ H ₅	26	171	C ₁₆ H ₁₃ N ₃ S	14.78, 14.77	15.05	11.43, 11.36	11.46
XXVIII	CH ₂ CH ₂ COOH	35	182 (dec.)	C ₁₂ H ₁₁ O ₂ N ₃ S			11.93, 11.80	12.29
XXIX	OH	70	>300	C ₉ H ₇ ON ₃ S • H ₂ O			14.28, 14.37	14.34
XXX	SH	51	>300	C ₉ H ₇ N ₃ S ₂			28.75, 28.74	28.95

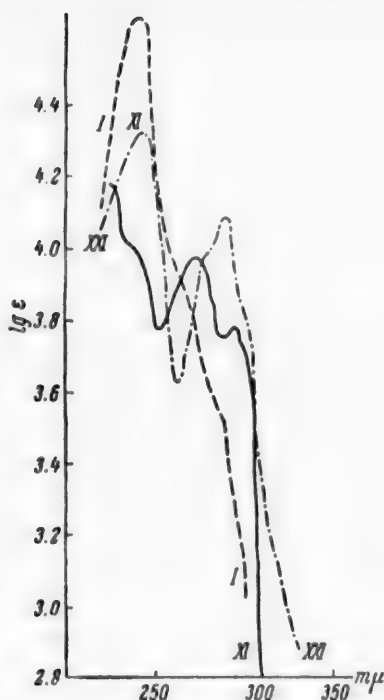
TABLE 2

Prep. No.	λ_{\max} (in mμ)	lg ε
I	242	4.64
XI	272, 294	3.96, 3.78
XXI	241, 288	4.33, 4.08

Condensation of o-diamino derivatives of 2-methylbenzothiazole with formic, acetic, propionic, glycolic, lactic, and succinic acids was effected by boiling the components in 15% hydrochloric acid. Condensation of benzoic acid in 25% hydrochloric acid in sealed tubes goes unsatisfactorily; 2-phenyl derivatives of thiazolobenzimidazole were therefore prepared by reactions of diamines with benzaldehyde in nitrobenzene by the procedure recently put forward for synthesis of 2-phenyl-5,6-dichlorobenzimidazole [3].

Condensation with phenylacetic acid was effected by fusion of the components at 125–130°. 2-Hydroxy derivatives of thiazolobenzimidazoles were obtained by fusion of diamino-2-methylbenzothiazoles with urea; 2-mercapto derivatives were obtained by boiling with carbon disulfide in alcoholic solution.

The thiazolobenzimidazoles that we synthesized are listed in Table 1. They are colorless, crystalline compounds melting at above 100°. Fusion of the thiazole nucleus to the benzimidazole system is largely responsible



Absorption curves of thiazolobenzimidazoles (I), (XI), and (XXI).

for the rise in melting point. For example, benzimidazole melts at 170° , while thiazolobenzimidazoles melt at 213° (I), $297-298^{\circ}$ (XI), and 283° (XXI). The majority of the thiazolobenzimidazoles have good solubility in hot water and in alcohol, while the 2-alkyl derivatives are soluble also in benzene and ether. All of the thiazolobenzimidazoles are readily soluble in dilute hydrochloric acid. In this connection, it should be noted that derivatives of the linear isomer are distinguished by greater solubility in water and organic solvents than derivatives of the angular isomers. Thiazolobenzimidazoles readily form dihydrochlorides and picrates.

The ultraviolet absorption maxima of the thiazolobenzimidazoles not substituted in the imidazole ring are presented in Table 2.

The absorption curves of the above thiazolobenzimidazoles are plotted in the figure. Measurements were made on alcoholic solutions.

EXPERIMENTAL

7-Methylthiazolo(4,5-g)benzimidazole (I). A mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole, 1 ml of formic acid, and 20 ml of 15% hydrochloric acid was boiled for 2 hr, whereupon the cooled solution was filtered and neutralized with ammonia solution. The white precipitate was recrystallized from water (weight 0.56 g). Colorless needles, readily soluble

in hot water, alcohol, and dilute hydrochloric acid, insoluble in benzene and ether.

Picrate: yellow needles (from alcohol) with m.p. $274-275^{\circ}$ (decomp.).

Found %: S 7.45, 7.57. $C_{15}H_{10}O_7N_6S$. Calculated %: S 7.65.

7-Methylthiazolo(5,4-g)benzimidazole (XII). Prepared similarly from 2-methyl-4,5-diaminobenzothiazole. Recrystallized from alcohol.

Picrate: yellow needles (from methanol), m.p. 233° (decomp.).

Found %: S 7.67, 7.43. $C_{15}H_{10}O_7N_6S$. Calculated %: S 7.65.

6-Methylthiazolo(4,5-f)benzimidazole (XXI). Prepared similarly from 2-methyl-5,6-diaminobenzothiazole. Recrystallized from aqueous alcohol. Firmly retains two molecules of water.

Picrate: yellow needles (from methanol), m.p. 234° .

Found %: N 19.93, 19.83; S 7.76, 7.57. $C_{15}H_{10}O_7N_6S$. Calculated %: N 20.09; S 7.65.

Preparations (II)-(V), (XII)-(XV), (XXI)-(XXV) were obtained under the same conditions. Preparations (II), (III), (IV), (XXIV), and (XXV) were recrystallized from water, and preparations (V), (XI), (XII), (XIII), (XXI), and (XXII) from 70% alcohol.

2,7-Dimethylthiazolo(4,5-g)benzimidazole (II) picrate: yellow needles (from alcohol) with m.p. 246° (decomp.).

Found %: N 19.23, 19.22; S 7.31, 7.44. $C_{18}H_{12}O_7N_6S$. Calculated %: N 19.44; S 7.40.

The dihydrochloride of (II) was prepared by addition of ethereal hydrogen chloride to a solution of the base in absolute alcohol. The white precipitate was filtered, washed repeatedly with dry ether, and dried in a vacuum desiccator. M.p. $346-347^{\circ}$ (decomp.).

Found %: Cl 25.82, 25.55. $C_{10}H_8N_3S \cdot 2HCl$. Calculated %: Cl 25.72.

2,6-Dimethylthiazolo(4,5-f)benzimidazole (XXII) picrate: yellow needles (from alcohol) with m.p. 246° (decomp.).

Found %: N 19.23, 19.22; S 7.31, 7.44. $C_{16}H_{12}O_7N_6S$. Calculated %: N 19.44; S 7.40.

The dihydrochloride of (XXII) was prepared similarly to dihydrochloride of (II); m.p. 298° (decomp.).

Found %: Cl 25.40, 25.55. $C_{16}H_{12}N_6S \cdot 2HCl$. Calculated %: Cl 25.72.

2-Ethyl-6-methylthiazolo(4,5-f)benzimidazole (XXIII): yellow needles (from methanol) with m.p. 238° (decomp.).

Found %: S 7.17, 7.30. $C_{17}H_{14}O_7N_6S$. Calculated %: S 7.17.

2-Phenyl-7-methylthiazolo(4,5-g)benzimidazole (VI). To a suspension of 0.7 g of 2-methyl-6,7-diaminobenzothiazole in 1.5 ml of alcohol was added 0.43 g of benzaldehyde; after 2 min. the mixture was heated to 50°. The initially formed yellow solution deposited a yellow precipitate, to which was added 1.5 ml of nitrobenzene, whereupon the mixture was quickly heated to 200°; the resulting solution was held for 1 min at this temperature. Addition was then made (with cooling) of an ethereal solution of hydrogen chloride. The precipitated hydrochloride was filtered off, washed with ether, and dissolved in water. The residual nitrobenzene was extracted from the aqueous solution with ether, and the solution neutralized with sodium bicarbonate. The grayish precipitate was filtered, washed with water, and dried. Weight of precipitate 0.7 g. Colorless needles after two crystallizations from aqueous alcohol.

In similar fashion, preparation (XVI) was obtained from 2-methyl-4,5-diaminobenzothiazole and (XXVI) from 2-methyl-5,6-diaminobenzothiazole.

2-Benzyl-7-methylthiazolo(4,5-g)benzimidazole (VII). A thoroughly pulverized mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole and 0.7 g of phenylacetic acid was heated for 30 min at 125-130°. The resulting melt was dissolved in 20 ml of 15% hydrochloric acid; the solution was treated with carbon, and the filtrate neutralized with concentrated ammonia solution (ice cooling). The precipitate (0.4 g) was filtered, washed with water, and recrystallized from alcohol. Colorless needles.

In the same way, preparation (XVII) was obtained from 2-methyl-4,5-diaminobenzothiazole and (XXVII) from 2-methyl-5,6-diaminobenzothiazole.

7-Methylthiazolo(4,5-g)benzimidazole-2-propionic acid (VIII). A mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole, 0.5 g of succinic acid, and 15 ml of 15% hydrochloric acid was boiled for 3 hr. On cooling, a small quantity of solid (0.05 g) came down and was filtered. The filtrate was made alkaline with 40% sodium hydroxide solution. The resulting amorphous precipitate (0.01 g) melted above 300°. It was not examined more closely. The alkaline filtrate was made acid (to pH 6) with hydrochloric acid, and after long standing it deposited colorless crystals (0.56 g) which were recrystallized from water. Colorless needles, readily soluble in dilute sodium carbonate solution.

Preparations (XVIII) and (XXVIII) were similarly obtained from 2-methyl-4,5-diaminobenzothiazole and 2-methyl-5,6-diaminobenzothiazole.

2-Hydroxy-7-methylthiazolo(4,5-g)benzimidazole (IX). A thoroughly pulverized mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole and 0.6 g of urea was heated for 30 min on a paraffin wax bath at 150-155°. The melt was treated with hot water and filtered from the precipitate; the latter was dissolved in 5% sodium carbonate solution, the solution treated with carbon, and the filtrate acidified with acetic acid. The resulting snow-white needles (0.6 g) were readily soluble in alcohol and aqueous caustic alkali solution, poorly soluble in water.

Compounds (XIX) and (XXIX) were similarly prepared from 2-methyl-4,5-diaminobenzothiazole and 2-methyl-5,6-diaminobenzothiazole.

2-Mercapto-7-methylthiazolo(4,5-g)benzimidazole (X). A mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole, 1 g of carbon disulfide, and 20 ml of alcohol was boiled on a water bath for 3 hr. The white precipitate was filtered and washed with water and alcohol. For purification it was dissolved in 1% sodium hydroxide solution, filtered and acidified with acetic acid. Weight of precipitate 0.56 g. Sparingly soluble in alcohol.

Recrystallized from a large quantity of methanol for analysis.

Compounds (XX) and (XXX) were similarly prepared.

SUMMARY

Condensation of o-diamino derivatives of 2-methylbenzothiazole with carboxylic acids, urea, and carbon disulfide gave three series of isomeric thiazolobenzimidazoles: thiazolo(4,5-g)benzimidazoles, thiazolo(5,4-g)-benzimidazoles, and thiazolo(4,5-f)benzimidazoles.

Their properties were studied and their ultraviolet absorption spectra determined.

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ADDITION OF FULL ESTERS OF PHOSPHOROUS AND PHOSPHINOUS ACIDS TO CONJUGATED SYSTEMS

X. INTERACTION OF TRIALKYL PHOSPHITES WITH π, π, π -CONJUGATED SYSTEMS

V. A. Kukhtin and K. M. Orekhova

Kazan Branch of the Scientific Research Institute for Motion-Picture Photography

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May, 1960

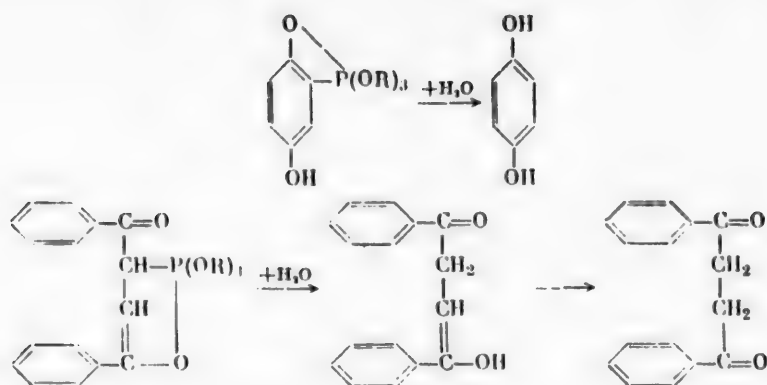
Original article submitted May 11, 1959

In communication [1] we described the addition of trialkyl phosphites to p-quinones — compounds possessing a π, π, π -conjugated system. In continuation of our work on reactions of trialkyl phosphites with such systems, we have studied their interaction with trans- and cis-dibenzoyl ethylene and vinylacrylic acid.

Triethyl phosphite starts to react with trans-dibenzoyl ethylene at room temperature, the temperature rising slightly. When the reaction was performed under mild conditions (in ethereal solution), removal of the solvent left a thick (glycerollike) product that did not crystallize on cooling, and did not distil without decomposition in high vacuum (1×10^{-2} mm). Examination of the unpurified substance showed it to possess the properties of the previously described intermediate products of addition of trialkyl phosphites to conjugated systems: It reacts with water with heat liberation, and initiates polymerization of acrylates. Under more drastic conditions (in a sealed tube at 100°), a product is obtained that no longer exhibits the properties of the intermediate product of addition. Even in this case, however, the end product could not be separated. Vacuum distillation yielded triethyl phosphate and a considerable quantity of 2,5-diphenylfuran. Cis-dibenzoyl ethylene reacts like the trans-form and the same results were obtained when its reactions were studied.

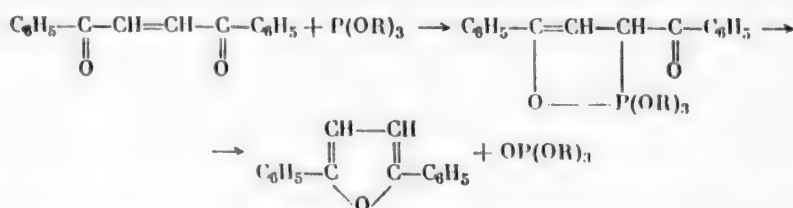
Treatment of the intermediate product of addition of triethyl phosphite to diphenyl ethylene with water gave dibenzoyl ethane as the main product. This result indicates that trialkyl phosphites, like p-quinones, add on to dibenzoyl ethane in the 1,4 position. In communication [1] it was pointed out that formation of hydroquinone is observed when phosphites act on p-quinone in wet benzene. This effect is evidently also associated with the action of water on the intermediate product of the reaction:

*Original Russian pagination. See C.B. translation.



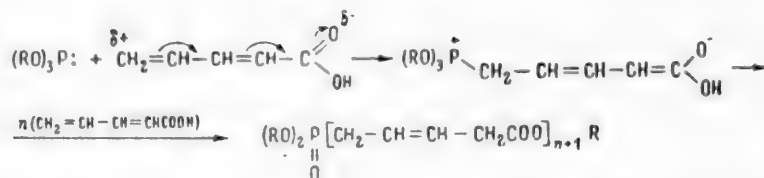
In the first case, the aromatic hydroquinone system is formed; in the second case, the double bond is hydrogenated.

Formation of 1,4-diphenylfuran is probably the result of thermal breakdown of the intermediate addition product. The over-all reaction may be expressed by the following equation:



Another possibility is the formation of 1,4-diphenylfuran by thermal dehydration of the diphenylethane formed by the action of moisture on the intermediate product.

Vinylacrylic acid reacts less vigorously with trialkyl phosphites than acrylic and methacrylic acids [2]. We were unable to establish the formation of an intermediate reaction product as in the reactions with α, β -unsaturated acids [2] and aldehydes [3]. Only a minute quantity of phosphonovinylacrylic ester could be isolated after reaction of vinylacrylic acid with triethyl phosphite. The main reaction product is the telomer resulting from addition of several molecules of vinylacrylic acid to triethyl phosphite. Tripropyl phosphite and vinylacrylic acid form the telomer exclusively. The properties of the telomer are similar to those previously described [4]. In our opinion, the results can be explained as follows. Due to the difficulty of formation of the 7-membered cyclic intermediate product during the first step of the reaction, the dipolar ion is not stabilized in the intermediate product, but adds on another few molecules of acid so that the reaction acquires the character of a telomerization



The inability of vinylacrylic acid to form intermediate products of the Arbuzov rearrangement and the pattern of the reaction are consequently indirect confirmation of the covalent structure of the previously described intermediate products of reactions of phosphites with π, π -conjugated systems, since, if they possessed an ionic structure, we should have expected formation of intermediate products also in the present reaction.

EXPERIMENTAL

Reaction of triethyl phosphite with trans-dibenzoyl ethylene. Experiment 1. To 8 g of trans-dibenzoyl ethylene was added 6 g of triethyl phosphite. Reaction was effected in a sealed tube. After 30 min the whole of the dibenzoyl ethylene had dissolved in the triethyl phosphite. The temperature rose in course of dissolution.

The tube was thereupon heated for 5 hr at 120° (oil bath). Vacuum distillation yielded: 2 g (30.7%) of triethyl phosphate with b.p. 82-84° (5 mm), n_D^{20} 1.4060, and 4 g of 2,5-diphenylfuran with b.p. 138-142° (1.25×10^{-2} mm), m.p. 89-90°.

Found %: C 87.25, 87.25; H 4.92, 5.07. $C_{16}H_{12}O$. Calculated %: C 87.30; H 5.40.

Experiment 2. To an ethereal solution of 21 g of trans-dibenzoyl ethylene was added 15 g of triethyl phosphite. The reaction mixture was heated on a water bath for 5 hr at the boiling point of ether. The resulting product reacted with water with considerable heat liberation and initiated polymerization of methacrylic acid. The product did not distil in high vacuum, and did not crystallize.

Action of water on the intermediate reaction product. To 1 g of intermediate product was added 0.04 g of water. Vigorous shaking lead to a temperature rise of 25°. Crystals (0.4 g) came down which had m.p. 141-142° after numerous recrystallizations from absolute alcohol [5]. The product gave a green coloration with concentrated sulfuric acid, which is characteristic of dibenzoyl ethane.

Addition of triethyl phosphite to cis-dibenzoyl ethylene. To 3 g of cis-dibenzoyl ethylene was added 2.1 g of triethyl phosphite. The reaction mixture was heated in a sealed tube at 90° for 10 hr. Vacuum distillation gave 2.1 g of 2,5-diphenylfuran with b.p. 240-245° (10 mm), m.p. 88-89°. No depression of melting point in admixture with diphenylfuran prepared by reaction of triethyl phosphite with trans-dibenzoyl ethylene.

Addition of triethyl phosphite to vinylacrylic acid. To an ethereal solution of 7 g of vinylacrylic acid, stabilized with hydroquinone, was added 11.8 g of triethyl phosphite. The temperature rose by 2°. The reaction mixture was heated on a water bath for 15 hr. Vacuum distillation gave 1 g (5.9%) of the ethyl ester of (diethylphosphono)-butene-2-carboxylic acid.

B.p. 172-175° (15 mm), n_D^{20} 1.4490, d_4^{20} 1.0842.

Literature data [6]: b.p. 174-176° (18 mm), n_D^{20} 1.4489, d_4^{20} 1.0851.

The residue was a polymeric mass which contained 3.4% of phosphorus after repeated washing with ether. Similar results were obtained in further experiments under various conditions.

SUMMARY

1. A study was made of the reaction of triethyl phosphite with dibenzoyl ethylene. It was found that dibenzoyl ethylene reacts like p-quinones with trialkyl phosphites.

2. The interaction of trialkyl phosphites with vinylacrylic acid was studied. Unlike unsaturated acids, vinylacrylic acid reacts mainly with formation of phosphorus-containing telomers.

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*Original Russian pagination. See C.B. translation.

INVESTIGATIONS IN THE IMIDAZOLE SERIES

VIII. SYNTHESIS OF SOME DERIVATIVES OF IMIDAZOLECARBOXYLIC AND IMIDAZO-(2,1-b)-THIAZOLECARBOXYLIC ACIDS*

P. M. Kochergin

S. Ordzhonikidze All-Union Research Institute of Chemical Pharmaceutics

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The preparation of some derivatives of imidazole- and imidazo-(2,1-b)-thiazolecarboxylic acids was of interest in connection with biological investigations.

Imidazole-(5,4)- and 2-mercaptoimidazole-5(4)-carboxylic acids (VII and V), and their ethyl esters (VI and IV) were prepared by the literature methods [1,2]; at the same time, the procedure for some of the compounds was improved, and data for some properties (melting point, character of crystals, and solubility) were revised. It was observed that the methyl ester of 2-mercaptoimidazole-5(4)-carboxylic acid (IX) is obtained by reaction of ethyl N-formylglycinate (II), methyl formate, and sodium methoxide, followed by condensation of the intermediate enolate with potassium thiocyanate in presence of hydrochloric acid. In this case, the Claisen reaction apparently results in transesterification of (II) to the methyl ester of N-formylglycerine. In order to exclude the possibility of such a transesterification in the preparation of (IV), we did not use sodium methoxide (as recommended in the literature [1]), but sodium ethoxide, as practiced in a patent [3]. For preparation of (VI) by oxidation of (IV) we decided to use not nitric acid, but hydrogen peroxide. However, this led, in contrast to the outcome of oxidation of other derivatives of 2-mercaptoimidazole [4-6], to formation of the corresponding disulfide.

Later we studied the action of α -halocarbonyl compounds on the ethyl and methyl esters of 2-mercaptoimidazole-5(4)-carboxylic acids (IV and IX) (see scheme on following page).

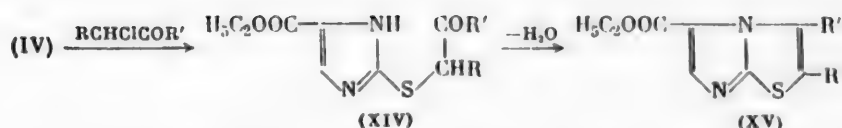
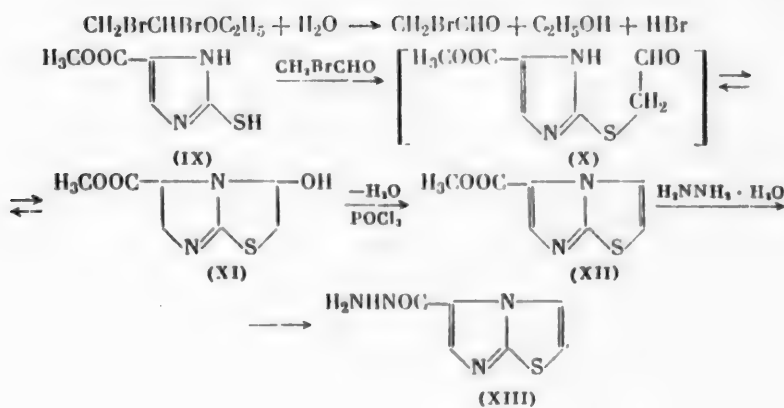
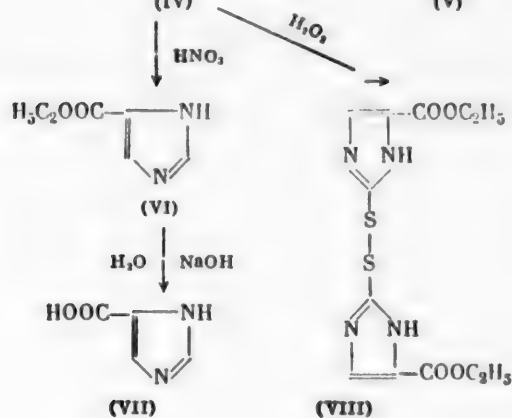
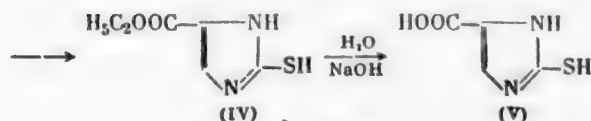
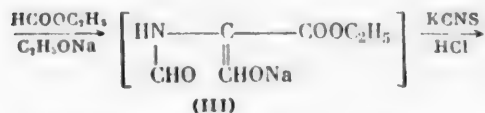
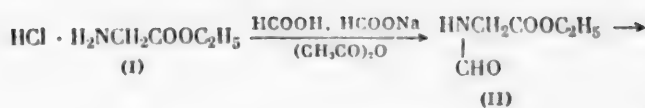
Reaction of mercaptan (IX) with bromoacetaldehyde in aqueous solution gave a crystalline compound which, by analogy with 3-hydroxy-6-phenylimidazo-(2,1-b)-thiazoline [7], probably has the structure of the methyl ester of 3-hydroxyimidazo-(2,1-b)-thiazoline-5-carboxylic acid (XI). Hydroxy compound (XI) evidently undergoes partial transition into 5(4)-carbomethoxyimidazolyl-2-mercaptoacetaldehyde (X) in solution, as indicated by its reaction with fuchsin-sulfurous acid (the originally colorless solution turns crimson on standing). Compound (XI) reacts with hydrazine hydrate, but no crystalline compounds could be isolated from the reaction products. Phosphorus oxychloride acts on hydroxy compound (XI) with detachment of a molecule of water to give the methyl ester of imidazo-(2,1-b)-thiazole-5-carboxylic acid (XII). Reaction of methyl ester (XII) with hydrazine hydrate gave the corresponding hydrazide (XIII) (see scheme on following page).

Reaction of mercaptan (IV) with α -haloketones (chloroacetone, 3-chloro-2-butanone, 3-chloro-2,4-pentanedione, α -bromoacetophenone) in ethanol gave the ethyl esters of 2- β -ketoalkyl(aryl)-mercaptoimidazole-5(4)-carboxylic acids (XIV). The latter lose water to form bicyclic compounds - ethyl esters of the corresponding imidazo-(2,1-b)-thiazole-5-carboxylic acids (XV).

Cyclization of ketones (XIV) to bicyclic compounds (XV) was effected with the help of water-binding agents (phosphorus oxychloride or concentrated sulfuric acid) and, in some cases, by boiling of the hydrochlorides of (XIV) in butanol (see scheme on following page).

I place on record my sincere thanks to M. N. Shchukina for her valuable advice during the present investigation.

*Communication VII: Zhur.Obshch. Khim., 26, 2916 (1956). [See C.B. translation.]



a) $\text{R} = \text{H}, \text{R}' = \text{CH}_3$; b) $\text{R} = \text{R}' = \text{CH}_3$; c) $\text{R} = \text{COCH}_3, \text{R}' = \text{CH}_3$; d) $\text{R} = \text{H}, \text{R}' = \text{C}_6\text{H}_5$.

EXPERIMENTAL

Ethyl glycinate hydrochloride (I). The literature methods were slightly modified [8,9]. Dry hydrogen chloride was passed at 0° into a suspension of 300 g of glycine in 1700 ml of anhydrous ethanol for 18-20 hr. The mixture was then heated at the boil for an hour [compound (I) did not dissolve completely] and cooled to -8°. The precipitate was filtered, washed with ether, and dried to constant weight at 100°. Yield of (I), 536-556 g (95.9-99.6%) with m.p. 144°. The literature [8] gives m.p. 144°.

Methyl glycinate hydrochloride was similarly prepared. Yield 94.6-97.1%, m.p. 175°, in agreement with the literature [8].

Ethyl ester of N-formylglycine (II). Prepared as in [1]. Yield of pure, twice-distilled product 75-80%. A colorless liquid with b.p. 142-144° (12 mm), 156-157° (18 mm). Literature [1]: b.p. 110° (1 mm).

Ethyl ester of 2-mercaptoimidazole-5(4)-carboxylic acid (IV). Prepared as in [1]. Colorless prisms (from ethanol) with m.p. 184.5-185.5° (with foaming). According to [1]: m.p. 184°.

Methyl ester of 2-mercaptoimidazole-5(4)-carboxylic acid (IX). To a suspension (cooled to -15°) of 10.8 g of sodium methoxide in 100 ml of anhydrous ether was added the ethyl ester of N-formylglycine (24.2 g) and 33 g of methyl formate. After it had been stirred for an hour at -15°, the reaction mixture was stood in a refrigerator overnight at -20°. A gelatinlike brown precipitate came down. The ether was decanted off and the precipitate dissolved in 100 ml of water. Into the resulting solution, in the cold, were stirred 34.4 ml of 36% hydrochloric acid and 20.7 g of potassium thiocyanate, after which the solution was heated for 2 hr on a water bath at 70°. Cooling with ice brought down a yellow solid, which was filtered off, washed with water, and dried. Yield 15.1 g (51.6%) of substance with m.p. 172-174° (foaming); recrystallization from ethanol gave colorless plates with m.p. 182-183° (foaming); according to [1], the m.p. is 190-191°. A mixture with (IV) melted at 165-168°.

Found %: C 38.04; H 3.90; N 17.52; S 20.45. $C_6H_6O_2N_2S$. Calculated %: C 37.96; H 3.82; N 17.71; S 20.27.

2-Mercaptoimidazole-5(4)-carboxylic acid (V). A mixture of 10 g of ethyl ester (IV) and 20 ml of 24% aqueous sodium hydroxide was heated for an hour on a boiling water bath. The solution was then cooled and neutralized with 36% hydrochloric acid until the liquid was acid to Congo. The resulting precipitate, after cooling, was filtered, washed with water and then with acetone, and dried. There was obtained 5.5 g of substance with m.p. 226-227° (decomp.). Evaporation of the mother liquor to a small volume led to separation of an additional 1.8 g of the same substance. Total yield of (V), 7.3 g (87.2%). For analysis, the substance was recrystallized from water, then from alcohol. Colorless prisms (from ethanol) with m.p. 228-229° (decomp.); according to [2], the m.p. is 235-236° (decomp.); readily soluble in hot water, alcohol, and acetone; nearly insoluble in benzene, toluene, ether, chloroform, carbon tetrachloride, ethyl acetate, dioxane, and ligroline.

Found %: C 33.32; H 2.97; N 19.07; S 21.82. $C_4H_4O_2N_2S$. Calculated %: C 33.32; H 2.77; N 19.43; S 22.25.

Hydrolysis of ester (IX) under similar conditions gave an 85% yield of acid (V).

Sodium salt: colorless crystals (from water), sparingly soluble in cold water, easily soluble in hot water.

Found %: N 16.68. $C_4H_3O_2N_2SNa$. Calculated %: N 16.86.

Ethyl ester of imidazole-5(4)-carboxylic acid (VI). Prepared as in [1]. Yield of technical product (m.p. 157-159°) 80%. Recrystallization from a mixture of ethanol and ethyl acetate gave colorless plates with m.p. 162° (according to [1], m.p. 157-158°; according to [10], m.p. 162°), easily soluble in alcohol, sparingly soluble in ethyl acetate and acetone, nearly insoluble in benzene.

Imidazole-5(4)-carboxylic acid (VII). Prepared by the method of [1]. Colorless needles (from water), or fine prisms (from ethanol), m.p. 250-265°, with decomp. It melts sharply over a range of 0.5 to 1°; the melting point is markedly dependent on the duration of heating of the capillary. Sparingly soluble in organic solvents and cold water, easily soluble in hot water. According to [1], it has m.p. 271° (decomp.); according to [8], it has m.p. 275°.

Found %: C 42.97; H 3.92; N 25.40. $C_4H_4O_2N_2$. Calculated %: C 42.84; H 3.60; N 25.00.

Di-[5(4)-carbethoxyimidazolyl-2]disulfide (VIII). a) To a suspension of 1 g of mercaptan (IV) in 10 ml of water were added one drop of concentrated sulfuric acid and 3.5 ml of 12.6% hydrogen peroxide. The reaction was exothermic, and the original solid substance was transformed into another crystalline compound. On completion of the reaction, the mixture was cooled; the precipitate was filtered, washed with water, with aqueous sodium bicarbonate, then with water, and dried. There was obtained 0.75 g (75%) of a substance with m.p. 191 to 193° (decomp.). Recrystallization from alcohol gave colorless crystals with m.p. 199-200° (decomp.), soluble in alcohol, ethyl acetate, dioxane, chloroform, acetone, and concentrated solutions of hydrochloric acid and sodium hydroxide; sparingly soluble in benzene and toluene; insoluble in ether, benzene, water, and sodium bicarbonate solution. A mixture with (V) melted at 175-178°.

Found %: C 42.26; H 3.92; N 16.66; S 18.43. $C_{12}H_{14}O_4N_4S_2$. Calculated %: C 42.07; H 4.12; N 16.37; S 18.73.

b) To a solution of 1 g of (IV) in 20 ml of ethanol was added 3.5 ml of 12.6% hydrogen peroxide, and the mixture boiled for 25 min. To the hot solution was added sodium bicarbonate. Carbon dioxide came off. The solution was filtered and evaporated to dryness in vacuo to leave a crystalline residue which was washed with water and dried. Yield 0.5 g (50%) of substance with m.p. 192-194° (decomp.); recrystallization from alcohol gave colorless crystals with m.p. 199-200° (decomp.), not giving a depression of melting point in admixture with the product obtained by method a.

Methyl ester of 3-hydroximidazo-(2,1-b)-thiazoline-5-carboxylic acid (XI). A mixture of 4.2 g of α,β -dibromodiethyl ether and 15 ml of water was boiled for a few minutes, and then 2.8 g of mercaptan (IX) was added to the cooled solution; the mixture was heated for 30 min at 50-55°. The solution was cooled and neutralized with sodium bicarbonate; the resulting precipitate was filtered, washed with water, and dried. Yield 2.6 g (73.5%) of substance with m.p. 165-170° (decomp.); recrystallization from alcohol gave colorless needles with m.p. 172-174° (decomp.), soluble in the majority of organic solvents and in mineral acid solutions, sparingly soluble in ether and carbon tetrachloride, insoluble in water, ligroine, and cold aqueous caustic alkali. A mixture of an alcoholic solution of compound (XI) with an alcoholic solution of fuchsin-sulfurous acid (fuchsin II) formed a colorless solution which gradually turned crimson.

Found %: C 41.95; H 4.12; N 14.18; S 15.81. $C_7H_6O_3N_2S$. Calculated %: C 41.97; H 4.03; N 13.99; S 16.02.

Methyl ester of imidazo-(2,1-b)-thiazole-5-carboxylic acid (XII). To 4.2 g of ester (XI) was added 10 ml of phosphorus oxychloride (the operation was accompanied by heat liberation and foaming), and the solution was then boiled for 5 min. The phosphorus oxychloride was then distilled off in vacuo; water and an excess of sodium bicarbonate were added to the residue. The mixture was extracted with chloroform, the solution dried with magnesium sulfate, and the solvent taken off in vacuo. There was obtained 2.1 g (55%) of substance with m.p. 140 to 142° (decomp.); recrystallization from alcohol gave colorless crystals with m.p. 151-152° (with browning), soluble in the majority of organic solvents, hot water, and mineral acid solutions; sparingly soluble in cold water.

Found %: C 46.29; H 3.31; S 17.56. $C_7H_6O_2N_2S$. Calculated %: C 46.13; H 3.32; S 17.60.

Hydrochloride: colorless crystals (from alcohol) with m.p. 161-162° (decomp.).

Found %: Cl 16.48. $C_7H_6O_2N_2S \cdot HCl$. Calculated %: Cl 16.22.

Picrate: yellow needles (from alcohol) with m.p. 178-179°.

Found %: N 17.49. $C_{13}H_9O_9N_5S$. Calculated %: N 17.03.

Hydrazide of imidazo-(2,1-b)-thiazole-5-carboxylic acid (XIII). To a suspension of 1.8 g of ester (XII) in 10 ml of water was added 0.6 g of 85% hydrazine hydrate. A white precipitate formed after some time; it was filtered, washed with a little water, and dried. Yield 1.5 g (90%) of substance with m.p. 208-210° (decomp.); recrystallization from alcohol gave colorless needles with m.p. 215-216° (decomp.), soluble in the majority of organic solvents; insoluble in water.

Found %: C 39.43; H 3.40; S 17.74. $C_6H_6ON_4S$. Calculated %: C 39.53; H 3.32; S 17.60.

Ethyl ester of 2-acetylmercaptimidazole-5-carboxylic acid (XIVa). A solution of 3.65 g of mercaptan (IV) and 1.98 g of chloroacetone in 15 ml of alcohol was boiled for 5 min, after which the solvent was taken off completely (the final traces in vacuo). The crystalline residue was washed with ether and dried. There was obtained 5.5 g (98%) of hydrochloride with m.p. 146-148°; recrystallization from dichloroethane gave colorless plates with m.p. 150-151°, easily soluble in alcohol and water, nearly insoluble in chloroform and ethyl acetate, sparingly soluble in the cold in dioxane and dichloroethane.

Found %: Cl 13.31. $C_9H_{12}O_3N_2S \cdot HCl$. Calculated %: Cl 13.39.

Decomposition of the hydrochloride by aqueous sodium bicarbonate solution yielded the base in the form of fine, colorless prisms in druses with m.p. 110-111° (from water), easily soluble in organic solvents, sparingly soluble in cold water.

Found %: Cl 47.51; H 5.25; N 11.99; S 14.08. $C_9H_{12}O_3N_2S$. Calculated %: C 47.35; H 5.30; N 12.27; S 14.05.

Ethyl ester of 3-methylimidazo-(2,1-b)-thiazole-5-carboxylic acid (XVa). a) A mixture of 3.5 g of the hydrochloride of ketone (XIVa) and 20 ml of concentrated sulfuric acid was heated for 30 min on a water bath at 55-60°. The solution was then cooled, poured into 150 ml of water, neutralized with 40% aqueous sodium hydroxide until alkaline, and extracted with chloroform. The extract was washed with water and dried with potassium carbonate. Evaporation to dryness in vacuo left a residue of 2.25 g (81%) of technical product with m.p. 116-117° (from aqueous alcohol). Colorless prisms easily soluble in organic solvents, sparingly soluble in water. A mixture with ketone (IVa) melted at 74-77°.

Found %: C 51.95; H 4.58; N 13.38; S 14.87. $C_9H_{10}O_2N_2S$. Calculated %: C 51.41; H 4.79; N 13.32; S 15.25

b) A mixture of 5.6 g of mercaptan (IV) and 3 g of chloroacetone in 15 ml of butanol was boiled for 1 hr 20 min (the last 20 min in presence of active carbon). The solution was filtered from carbon and cooled. The resulting precipitate was filtered and washed with ether. The hydrochloride was dissolved in water and decomposed with sodium bicarbonate solution. The precipitate was filtered and washed with water. Colorless prisms with m.p. 116-117° (from aqueous ethanol), not giving a melting point depression in admixture with the product obtained by method a.

Ethyl ester of 2,3-dimethylimidazo-(2,1-b)-thiazole-5-carboxylic acid (XVb). A solution of 3.7 g of mercaptan (IV) and 2.3 g of 3-chloro-3-butanone in 28 ml of ethanol was boiled for 2 hr; the solution was then evaporated to dryness in vacuo. To the residual hydrochloride of ketone (XIVb) was added 15 ml of phosphorus oxychloride, and the mixture was heated for 30 min at 100°, and then at the boiling point for 10 min. The phosphorus oxychloride was taken off in vacuo, the residue dissolved in water, and the solution heated with active carbon, filtered, and neutralized with sodium bicarbonate. The solution was extracted with dichloroethane, and the extract washed with water and dried with magnesium sulfate. The solvent was taken off in vacuo to leave the base of ester (XVb) in the form of a light-brown, noncrystallizing oil, soluble in organic solvents, poorly soluble in water.

Picrate: yellow, spindle-shaped crystals with m.p. 155.5-156.5° (from ethanol), soluble in acetone, dichloroethane, and glacial acetic acid; sparingly soluble in water and alcohol.

Found %: C 42.28; H 3.07; N 15.59; S 7.13. $C_{16}H_{15}O_5N_5S$. Calculated %: C 42.38; H 3.33; N 15.45; S 7.07.

Ethyl ester of 2-(α -acetylacetyl)-mercaptimidazole-5(4)-carboxylic acid (IVc). To a hot solution of 4.8 g of (IV) in 25 ml of alcohol was added 3.75 g of 3-chloro-2,4-pentanedione and the mixture boiled for 25 min (the last 5 min in presence of active carbon). The solution was filtered and cooled, and the precipitated hydrochloride was filtered and decomposed with aqueous sodium acetate. The resulting base was in the form of yellow prisms with m.p. 193-194° (from alcohol), soluble in the majority of organic solvents, insoluble in water.

Found %: C 48.71; H 4.97. $C_{11}H_{14}O_4N_2S$. Calculated %: C 48.88; H 5.22.

Ethyl ester of 2-acetyl-3-methylimidazo-(2,1-b)-thiazole-5-carboxylic acid (XVc). A solution of 2 g of the hydrochloride of diketone (XIVc) in 15 ml of butanol was boiled for an hour. On cooling, a crystalline hydrochloride came down and was filtered, washed with acetone, and decomposed with aqueous sodium acetate solution.

The base was obtained in the form of colorless, fine prisms with m.p. 157-158° (from alcohol), soluble in the majority of organic solvents, insoluble in water. A mixture with (XIVc) melted at 149-151°.

Found %: N 11.08; S 12.57. $C_{11}H_{12}O_3N_2S$. Calculated %: N 11.10; S 12.71.

Ethyl ester of 2-phenacylmercaptoimidazole-5(4)-carboxylic acid (XIVd). A solution of 5 g of mercaptan (IV) and 6.05 g of α -bromoacetophenone in 20 ml of alcohol was boiled for 40 min. A white precipitate soon started to come down during this operation. The mixture was cooled, and the precipitate filtered, washed with ether, and dried. There was obtained 10 g of substance with m.p. 192-193° (decomp.). Evaporation of the alcoholic mother liquor to a small volume led to separation of an additional 0.55 g of substance with m.p. 193-193.5° (decomp.). Total yield of hydrobromide 10.55 g (98%). Colorless plates with m.p. 195-196° (decomp.) (from ethanol), poorly soluble in water and alcohol.

Found %: Br 21.44. $C_{14}H_{14}O_3N_2S \cdot HBr$. Calculated %: Br 21.25.

The hydrobromide was dissolved in a large volume of hot water and decomposed with aqueous sodium bicarbonate. The precipitated base was filtered, washed with water, and recrystallized three times from ethanol (the first time with addition of carbon and a little dry sodium bicarbonate). Fine, colorless prisms with m.p. 127.5-128°, soluble in organic solvents, insoluble in water.

Found %: C 57.90; H 4.76; N 9.37; S 11.03. $C_{14}H_{14}O_3N_2S$. Calculated %: C 57.91; H 4.86; N 9.65; S 11.04.

Ethyl ester of 3-phenylimidazo-(2,1-b)-thiazole-5-carboxylic acid (XVd). A mixture of 4.1 g of hydrobromide of ketone (XIVd) and 15 ml of concentrated sulfuric acid was heated for 30 min at 70°, and then stood at room temperature for 36 hr. The solution was run into water and neutralized with sodium carbonate; the resulting precipitate was filtered, washed with water, and recrystallized from alcohol (containing carbon). Colorless prisms with m.p. 160-160.5° (decomp.), soluble in organic solvents, insoluble in water.

Found %: C 61.51; H 4.65; N 10.25; S 11.81. $C_{14}H_{12}O_2N_2S$. Calculated %: C 61.74; H 4.44; N 10.29; S 11.77.

SUMMARY

1. A series of esters of imidazo-(2,1-b)-thiazole-5-carboxylic acids was synthesized by reaction of methyl and ethyl esters of 2-mercaptoimidazole-5(4)-carboxylic acid with α -halocarbonyl compounds.
2. It was established that the corresponding disulfide is formed when the ethyl ester of 2-mercaptoimidazole-5(4)-carboxylic acid is oxidized with hydrogen peroxide.

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SOME PROPERTIES OF ESTERS OF DIALKYLARSINOUS ACIDS

Gil'm Kamai and B. D. Chernokal'skii

Kazan Institute of Chemical Technology

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We have reported [1] on the synthesis and some properties of esters of dialkylarsinous acids. The present work is a continuation of our investigations in this field.

As we showed earlier [1], the formation of trialkylalkoxyarsonium iodide is possible during synthesis of esters of dialkylarsinous acids from dialkyliodoarsines and sodium alkoxides. We tried to prepare the arsonium salt directly by reaction of the *n*-propyl ester of diethylarsinous acid with *n*-propyl iodide. Diethyl-*n*-propyl-*n*-propoxyarsonium iodide was actually formed. In aqueous solution the arsonium salt is fully dissociated into ions; the iodide anion titrates quantitatively with silver nitrate solution.

According to the literature [2,3], esters of alkylarsinous acids are oxidized to esters of alkylarsinic acids by selenium dioxide. Synthesis of esters of dialkylarsinic acids by a similar method appeared to us not without interest. Outwardly, the oxidation of esters of dialkylarsinous acids proceeds in the same way as that of esters of alkylarsinous acids, but during the first distillation a considerable proportion of the product resinifies and the consistency of the liquid alters. Performance of the first distillation at 13-15 mm leads not to the desired ester, but to the original substance (Nos. 1 and 2 in Table 1). Lowering of the pressure to 4 mm enables isolation of the *n*-butyl ester of diethylarsinic acid. The yield of ester of dialkylarsinic acid increases if the solvent is removed, after oxidation, at reduced pressure (Nos. 4 and 5 in Table 1).

From the distillate and resinous residue from the first distillation were isolated, apart from ester of dialkylarsinic acid, a series of products not observed during synthesis of esters of alkylarsinic acids. In all cases, for example, dialkylarsinic acid is obtained, and in two cases (2 and 5 in Table 1), an alcohol containing the radical entering into the alkoxy group of the original compound. From the products of oxidation of the *n*-butyl ester of diethylarsinous acid was isolated the di-*n*-butyl ester of ethylarsinous acid.

Formation of ester of alkylarsinous acid (No. 3 in Table 1), and the change of properties of the substances during the first distillation, led us to the idea that pyrolysis of the initially formed esters of dialkylarsinic acids might take place during their isolation. This hypothesis was confirmed by pyrolysis of the *n*-butyl ester of methyl-*n*-butylarsinic acid, since we isolated analogous products from the pyrolyzate: *n*-butyl alcohol and the *n*-butyl ester of methyl-*n*-butylarsinic acid.

The facility with which the $R_2As(OXOR) \rightarrow R_2AsOR$ transformation takes place evidently also accounts for the separation of esters of arylalkylarsinous acids on reaction of alkyl halides with silver salts of the corresponding arsinic acids [4].

Esters of dialkylarsinic acids are isolated in small yields when esters of dialkylarsinous acids are oxidized with selenium dioxide. We therefore made experiments with other oxidants. Direct reaction of dry oxygen with the *n*-propyl ester of methyl-*n*-butylarsinous acid gave methyl-*n*-butylarsinic acid. Mercuric oxide showed promise as an oxidant: its interaction with the ethyl ester of di-*n*-propylarsinous acid gave the ethyl ester of di-*n*-propylarsinic acid in comparable yield (Table 2).

The synthesized esters of dialkylarsinic acids (Table 2) are colorless liquids with a faint odor, easily hydrolyzed by water and by moisture of the air. Our calculations give an atomic refraction of arsenic in these compounds of 8.19.

TABLE 1

Oxidation of Esters of Dialkylarsinous Acids with Selenium Dioxide

Prep No.	Starting ester	Substance obtained	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Yield (in %)
1	$(C_2H_5)_2AsOC_2H_5$	$(C_2H_5)_2AsOC_2H_5$ $(C_2H_5)_2As(O)(OH)$	140–141° m.p. 136–137°	1.1148 —	1.4630 —	2.1 1.5
2	$(C_2H_5)_2AsOC_3H_7$	C_3H_7OH * $(C_2H_5)_2AsOC_3H_7$ $(C_2H_5)_2As(O)(OH)$	54.5–57 (13) m.p. 135–137	1.0904 —	1.4621 —	16.6 6.2 2.7
3	$(C_2H_5)_2AsOC_4H_9$	$C_2H_5As(OC_4H_9)_2$ $(C_2H_5)_2As(O)(OC_4H_9)$ $(C_2H_5)_2As(O)(OH)$	98.5–101 (11) 130–130.5 (4) m.p. 136–137	— 1.1922 —	1.4522 1.4721 —	2.0 12.1 11.9
4	$(CH_3)(C_4H_9)AsOC_2H_5$	$(CH_3)(C_4H_9)As(O)(OC_2H_5)$ $(CH_3)(C_4H_9)As(O)(OH)$	110–111 (2) m.p. 126–127	1.2265 —	1.4729 —	26.0 11.1
5	$(CH_3)(C_4H_9)AsOC_4H_9$	C_4H_9OH * $(CH_3)(C_4H_9)AsOC_4H_9$ $(CH_3)(C_4H_9)As(O)(OC_4H_9)$ $(CH_3)(C_4H_9)As(O)(OH)$	116–118 82.5–84 (10) 133–134 (3) m.p. 126–127	— 1.0461 1.1507 —	— 1.4588 1.4676 —	1.9 2.6 24.9 5.5

* Identified as ester of 3,5-dinitrobenzoic acid.

TABLE 2

Esters of Dialkylarsinic Acids

Prep. No.	Ester	Oxidant	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR _D	AR _D arsenic	Yield (%)
1	$(C_2H_5)_2As(O)(OC_4H_9)$	SeO ₂	130–130.5 (4)	1.1922	1.4721	52.19	8.09	12.1
2	$(CH_3)(C_4H_9)As(O)(OC_2H_5)$	SeO ₂	110–111 (2)	1.2265	1.4729	47.59	8.11	26.0
3	$(CH_3)(C_4H_9)As(O)(OC_4H_9)$	SeO ₂	133–134 (3)	1.1507	1.4676	57.01	8.29	24.9
4	$(C_3H_7)_2As(O)(OC_2H_5)$	HgO	116.5–118 (3)	1.1865	1.4718	52.36	8.16	18.8
Mean							8.19	

EXPERIMENTAL

Preparation of n-propyl ester of methyl-n-butylarsinous acid. Into a flask fitted with a reflux condenser were charged 30 g of anhydrous n-propyl alcohol and 15.43 g of bis(methyl-n-butylarsyl) oxide. Between flask and reflux condenser was inserted an adapter with a funnel containing anhydrous copper sulfate, so that the condensate passed through the funnel after running down from the condenser. After 3-hr heating, the excess alcohol was distilled off, and the residue was distilled to give 12.31 g (60%) of n-propyl ester of methyl-n-butylarsinous acid.

B.p. 73.5–75° (12 mm), d_4^{20} 1.0584; n_D^{20} 1.4575, MR_D 53.10. C₈H₁₉OAs. Calculated 53.05.

Found %: As 36.31. C₈H₁₉OAs. Calculated %: As 36.34.

Reaction of n-propyl iodide with n-propyl ester of diethylarsinous acid. A mixture of 1.83 g of n-propyl ester of diethylarsinous acid and 1.62 g of n-propyl iodide was stood in a sealed ampoule for 45 days at room temperature. The reaction mixture deposited 0.85 g (24.6%) of acicular crystals. Volume contraction occurred during reaction. The crystals were collected, washed with anhydrous benzene, and dried at reduced pressure. The diethyl-n-propyl-n-propoxyarsonium iodide melted at 241–243°.

Found %: As 20.19; I 35.21. $C_{10}H_{24}O_4As$. Calculated %: As 20.69; I 35.05.

Iodine was determined by titration of an aqueous solution of the arsonium salt with silver nitrate solution. The equivalence point was determined by high-frequency conductimetry.

Oxidation of ethyl ester of diethylarsinous acid with selenium dioxide. To a mixture of 19.98 g of selenium dioxide and 600 ml of dry benzene (heated to boiling) was added 53.31 g of ethyl ester of diethylarsinous acid. The reaction mixture was heated for 3 hr and then cooled; the deposited selenium was separated, and the solvent distilled off from the filtrate. Distillation of the rather viscous residue gave a fraction with b.p. 116-131° (15 mm). During the subsequent distillation, the liquid boiled at 35-61° (13 mm); crystals came down in the distillation flask; weight 0.75 g (1.5%), m.p. 136-137° (from n-butyl alcohol). According to the literature [5], diethylarsinic acid melts at 133-134°.

After redistillation, the product was a readily mobile liquid with a sharp, garliclike odor. Several distillations in vacuo gave 1.07 g (2.1%) of product.

B.p. 140-141°, d^{20}_4 1.1148, n^{20}_D 1.4600.

The ethyl ester of diethylarsinous acid previously obtained by us [1] had b.p. 141-142°, d^{20}_4 1.1114, n^{20}_D 1.4621.

Oxidation of n-propyl ester of diethylarsinous acid with selenium dioxide. Reaction of 12.21 g of selenium dioxide with 33.02 g of n-propyl ester of diethylarsinous acid in 400 ml of anhydrous benzene was performed as in the preceding preparation. A viscous liquid with b.p. 124° (15 mm) came over at first during vacuum distillation; toward the close of distillation the liquid became less viscous, and the boiling point fell to 108° at the same pressure. After standing, the distillate deposited crystals with m.p. 135-137° (from n-butyl alcohol). Diethylarsinic acid melts at 133-134° [5]. Fractional distillation of the distillate gave the following fractions:

1st, 1.71 g (16.6%), b.p. 95-105°. Reaction [6] with 3,5-dinitrobenzoyl chloride yielded crystals with m.p. 69-71° [7]. A mixture with the n-propyl ester of 3,5-dinitrobenzoic acid melted at the same temperature.

2nd, 2.06 g (6.2%), with b.p. 54.5-57° (13 mm), d^{20}_4 1.0904, n^{20}_D 1.4621.

The n-propyl ester of diethylarsinous acid [1] boils at 50-52° (10 mm), d^{20}_4 1.0859, n^{20}_D 1.4613.

Oxidation of n-butyl ester of diethylarsinous acid with selenium dioxide. Reaction of 50.34 g of n-butyl ester of diethylarsinous acid with 15.65 g of selenium dioxide in 525 ml of anhydrous benzene was effected by the previous procedure. After the solvent had been removed the residue deposited crystals which were filtered, washed with benzene, and dried. M.p. 136-137°, yield 4.81 g (11.9%).

A first fractionation of the filtrate was carried out at 4 mm; the following substances were obtained after redistillations:

I. 0.69 g (2%) of di-n-butyl ester of ethylarsinous acid with b.p. 98.5-101° (11 mm), n^{20}_D 1.4522.

Found %: As 30.04. $C_{10}H_{23}O_2As$. Calculated %: As 29.94.

Reaction with hydrogen iodide gave a brown, oily liquid with b.p. 126.5° (12 mm). According to the literature [8], ethyldiiodoarsine boils at 126° (11 mm).

II. 6.58 g (12.1%) of n-butyl ester of diethylarsinic acid.

B.p. 130-130.5° (4 mm), d^{20}_4 1.1922, n^{20}_D 1.4721, MR_D 52.19, AR_D of arsenic 8.09.

Found %: As 33.66. $C_8H_{19}O_2As$. Calculated %: As 33.73.

Oxidation of ethyl ester of methyl-n-butylarsinous acid with selenium dioxide. Using the same procedure, arsinous acid was oxidized with 10.10 g of selenium dioxide in 325 ml of anhydrous benzene. The selenium was separated. The solvent was suction filtered. Two distillations of the residue gave 7.09 g (26%) of ethyl ester of methyl-n-butylarsinic acid.

B.p. 110-111° (2 mm), d^{20}_4 1.2265, n^{20}_D 1.4729, MR_D 47.59, AR_D of arsenic 8.11.

Found %: As 36.17. $C_7H_{17}O_2As$. Calculated %: As 35.97.

Crystals with m.p. 126-127° (from butanol) were isolated from the resinous residue after the first distillation. Their analysis corresponded to methyl-n-butylarsinic acid. Yield 2.62 g (11.1%).

Found %: As 41.69. $C_5H_{13}O_2As$. Calculated %: As 41.60.

Oxidation of n-butyl ester of methyl-n-butylarsinous acid with selenium dioxide. Reaction of 56.77 g of ester with 16.98 g of selenium dioxide in 550 ml of anhydrous benzene in the usual manner gave (after numerous distillations), the following compounds:

I. 2.27 g (6.1%) of n-butyl alcohol, b.p. 116-118°. Reaction [4] with 3,5-dinitrobenzoyl chloride gave crystals with m.p. 62-63°; a mixture with n-butyl 3,5-dinitrobenzoate melted at the same temperature [7].

II. 15.14 g (24.9%) of n-butyl ester of methyl-n-butylarsinic acid.

B.p. 133-134° (3 mm), d^{20}_4 1.1507, n^{20}_D 1.4676, M_R 57.01, A_R of arsenic 8.29.

Found %: As 31.60. $C_9H_{21}O_2As$. Calculated %: As 31.72.

The residue after the first distillation gave 2.58 g (5.5%) of methyl-n-butylarsinic acid with m.p. 126-127° (from butanol).

Oxidation of n-propyl ester of methyl-n-butylarsinous acid with oxygen. Dry nitrogen was bubbled for 2 hr through 12 g of n-propyl ester of methyl-n-butylarsinous acid. The resulting fine, colorless crystals were filtered, washed with anhydrous ether, and dried. M.p. 127-128°, in agreement with that of ethyl-n-butylarsinic acid. From the filtrate was isolated 8.3 g of the original n-propyl ester of methylbutylarsinous acid.

Oxidation of ethyl ester of di-n-propylarsinous acid with mercuric oxide. A mixture of 37.5 g of mercuric oxide and 17.8 g of ethyl ester of di-n-propylarsinous acid in 250 ml of chloroform was heated for 40 hr with vigorous stirring. The liquid was decanted from the deposited mercury, and the chloroform distilled off. Distillation of the residue yielded 9.3 g of a 141-146° (11 mm) fraction. A small quantity of metallic mercury came down from the distillate. Redistillation gave 3.6 g (18.8%) of ethyl ester of di-n-propylarsinic acid.

B.p. 116.5-118° (3 mm) d^{20}_4 1.1865, n^{20}_D 1.4718, M_R 52.36, A_R of arsenic 8.26.

The ethyl ester of di-n-propylarsinic acid forms a colorless, viscous liquid with a faint odor, extremely easily hydrolyzed by water.

Pyrolysis of n-butyl ester of methyl-n-butylarsinous acid. Heating of 14.28 g of ester in a distillation flask to 210-280° led to distillation of 8.51 g of liquid; the residue (5.07 g) resinified. Two fractions were obtained on redistillation:

1st, 4.94 g, a colorless liquid with b.p. 28-33° (12 mm). Redistillation gave 2.65 g (30.4%) of n-butyl alcohol with b.p. 114.5-116.5°. Reaction [6] with 3,5-dinitrobenzoyl chloride gave a substance identical with n-butyl 3,5-dinitrobenzoate. Reaction of the broad cut with 2,4-dinitrophenylhydrazine in a mixture of alcohol and phosphoric acid gave fine, yellow needles. The hydrazone could not be isolated in the pure form.

2nd, 0.31 g (2.4%) of substance with b.p. 81-83° (11 mm), n^{20}_D 1.4612.

The n-butyl ester of methyl-n-butylarsinous acid that we had previously obtained [1] had b.p. 83° (10 mm), n^{20}_D 1.4603.

SUMMARY

1. A procedure was advanced for preparation of alkyl esters of dialkylarsinic acids by oxidation of the corresponding esters of dialkylarsinous acid with selenium dioxide.

2. The first representatives of the series of esters of dialkylarsinic acids were prepared, and the atomic refraction of arsenic in these compounds was calculated.

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SULFONATION OF β -DIKETONES

VII. CRYSTALLOGRAPHIC AND X-RAY INVESTIGATIONS OF ALKALI METAL AND AMMONIUM SALTS OF 3-INDANEDIONE-2-SULFONIC ACID

A. Ievinš, S. K. Apinītis, E. Gudriniece, and G. Vanags

Riga Polytechnic Institute

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It was shown in previous communications [1,2] that 1,3-indanedione-2-sulfonic acid forms well-crystallized alkali metal salts. The latter are colorless or slightly yellowish substances, perfectly stable in the air. They are readily soluble in water and sparingly in alcohol; their solubility decreases with increasing cationic radius. Crystals suitable for examination are obtained by crystallization from dilute ethanol. For crystallographic characterization the crystals were measured with a two-circle goniometer, and the approximate parameters of the unit cell determined from the distances between layer lines of powder photographs around the crystallographical axes.

TABLE 1

Spherical Coordinates of Faces of a Crystal of Lithium Salt of 1,3-Indanedione-2-sulfonic Acid

Symbol	φ	ρ	No. of measurements
100	$90^{\circ}01' \pm 11'$	$89^{\circ}56' \pm 6'$	6
010	$-27^{\circ}3' \pm 13'$	$89^{\circ}56' \pm 6'$	6
001	$-67^{\circ}43' \pm 27'$	$55^{\circ}24' \pm 25'$	6

Lithium salt of 1,3-indanedione-2-sulfonic acid $C_9H_5O_5SLi$. Preparation of good crystals was rather difficult due to the fairly high solubility. The {100} face was well developed (Fig. 1). Results of measurements with a two-circle goniometer are set forth in Table 1.

We see that the crystals belong to the pinacoidal class of triclinic syngony. In the present case, we have a combination of first, second, and third pinacoids. The inverse angles between the axes were calculated from the spherical coordinates of the faces: $\alpha^* = 128^{\circ}38' \pm 26'$; $\beta^* = 40^{\circ}23' \pm 26'$; $\gamma^* = 117^{\circ}3' \pm 16'$, which correspond to $\alpha = 61^{\circ}12' \pm 45'$; $\beta = 133^{\circ}22' \pm 34'$; $\gamma = 92^{\circ}22' \pm 42'$.

For approximate determination of the unit cell parameters of the crystals, x-ray powder photographs were taken, using copper radiation, around [100], [010], and [001], and the following values of the unit cell parameters were obtained from the distances between the planes: $a = 15.25$ kX; $b = 7.61$ kX; $c = 7.42$ kX. The pycnometric specific gravity (in toluene) was $d_{20} = 1.666$ g/ml.

The following data were calculated from the parameters found.

1. Ratio of roentgenographic axes:

$$a : b : c = 2.004 : 1 : 0.975.$$

*Original Russian pagination. See C.B. translation.

**Name not verified.

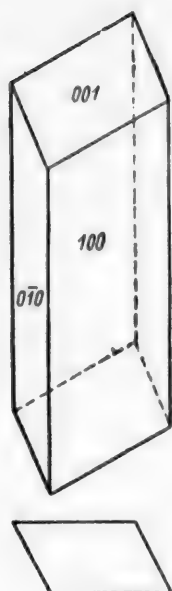


Fig. 1. Crystal of lithium salt of 1,3-indanedione-2-sulfonic acid.

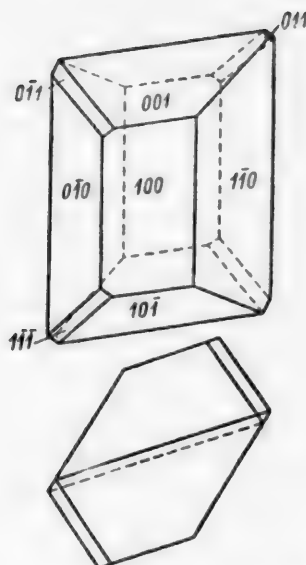


Fig. 2. Crystal of sodium salt of 1,3-indanedione-2-sulfonic acid (monohydrate).

2. Volume of unit cell:

$$V = abc \sin \beta \cdot \sin \gamma \cdot \sin \delta = 429.5 \text{ kX}^3,$$

$$\text{where } \sin \frac{\delta}{2} = \sqrt{\sin^2 \frac{\alpha - \beta + \gamma}{2} \sin^2 \frac{\alpha + \beta - \gamma}{2}}.$$

3. Number of molecules in unit cell:

$$z = \frac{V \cdot d \cdot N}{M} = \frac{429.5 \cdot 10^{-24} \cdot 1.626 \cdot 0.606 \cdot 10^{24}}{232.14} = 1.87 \sim 2.$$

Sodium salt of 1,3-indanedione-2-sulfonic acid with one molecule of water $C_{10}H_5O_5SNa \cdot H_2O$. Prepared by crystallization from relatively concentrated solutions in alcohol or dioxane. Specific gravity of crystals d_{20} 1.626 g/ml. Results of crystal measurements in a two-circle, reflecting goniometer are shown in Table 2.

TABLE 2

Spherical Coordinates of Crystal Faces of Sodium Salt of 1,3-Indanedione-2-sulfonic Acid (Monohydrate)

Symbol	φ	ρ	No. of measurements
010	$-14^\circ 8' \pm 4'$	$90^\circ 00' \pm 2'$	11
100	$90^\circ 00' \pm 3'$	$90^\circ 00' \pm 2'$	11
001	$-79^\circ 21' \pm 20'$	$30^\circ 45' \pm 4'$	11
110	$51^\circ 21' \pm 2'$	$90^\circ 00' \pm 2'$	11
011	$28^\circ 23' \pm 12'$	$38^\circ 37' \pm 15'$	11
011	$-40^\circ 33' \pm 14'$	$50^\circ 27' \pm 5'$	11
101	$80^\circ 00' \pm 8'$	$32^\circ 46' \pm 15'$	11
111	$-50^\circ 5' \pm 6'$	$47^\circ 21' \pm 3'$	11

The measurements indicate that the crystals belong to the pinacoidal class of triclinic syngony. In form they are a combination of the eight pinacoids (see Fig. 2).

The reverse angles between the axes were calculated from the spherical coordinates: $\alpha^* = 102^\circ 23' \pm 10'$, $\beta^* = 59^\circ 50' \pm 5'$; $\gamma^* = 104^\circ 8' \pm 5'$, corresponding to $\alpha = 83^\circ 44' \pm 12'$; $\beta = 118^\circ 22' \pm 8'$; $\gamma = 80^\circ 42' \pm 8'$.

The ratio of the crystallographic axes was calculated from the coordinates of the (101) and (110) faces:

$$a : b : c = 0.774 : 1 : 0.805.$$

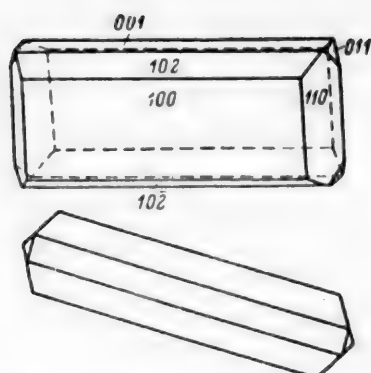


Fig. 3. Crystal of sodium salt of 1,3-indanedione-2-sulfonic acid (dihydrate).

The unit cell parameters were determined from powder photographs around [100], [010], and [001]:

$$a = 7.76 \text{ kX}; b = 10.03 \text{ kX}; c = 8.05 \text{ kX}.$$

The following additional values were calculated from the data found:

1. Ratio of roentgenographic axes:

$$a : b : c = 0.774 : 1 : 0.802.$$

2. Unit cell volume:

$$V = abc \cdot \sin \beta \cdot \sin \gamma \sin \delta = 516.0 \text{ kX}^3.$$

3. Number of molecules in unit cell:

$$z = \frac{V \cdot d \cdot N}{M} = \frac{516.0 \cdot 10^{-24} \cdot 1.626 \cdot 0.606 \cdot 10^{24}}{266.21} = 1.91 \sim 2.$$

Sodium salt of 1,3-indanedione-2-sulfonic acid dihydrate $C_9H_5O_5SNa \cdot 2H_2O$. Preparation of well-developed crystals is relatively difficult. Crystals suitable for measurements were obtained by recrystallization from dilute ethanol while cooling slowly. Results of measurements on 13 crystals are presented in Table 3. The crystals belong to the prismatic class of monoclinic syngony. The main forms are pinacoids {100}, {102}, {101}, {001}, and prisms {110} and {011}.

The ratio of the crystallographic axes was calculated from the coordinates of the (110) and (102) faces: $a:b:c = 1.785:1:2.201$. Monoclinic angle $\beta = 98^\circ 6' \pm 6'$.

TABLE 3

Spherical Coordinates of Faces of Crystals of Sodium Salt of 1,3-Indanedione-2-sulfonic Acid (Dihydrate)

Symbol	φ	ρ	No. of measurements
100	$90^\circ 00' \pm 3'$	$89^\circ 59' \pm 3'$	13
102	$90^\circ 00' \pm 3'$	$37^\circ 25' \pm 7'$	13
101	$90^\circ 00' \pm 3'$	$25^\circ 39' \pm 5'$	13
110	$29^\circ 30' \pm 7'$	$89^\circ 59' \pm 3'$	13
001	$90^\circ 00' \pm 3'$	$8^\circ 6' \pm 6'$	13

TABLE 4

Identity Periods of Sodium Salt of 1,3-Indanedione-2-sulfonic Acid (Dihydrate)

Direction of rotation	Identity period (in kX)	
	calc.	found
[110]	13.67	13.40
[101]	17.54	17.54
[011]	16.15	16.11

TABLE 5

Spherical Coordinates of Crystal Faces of Potassium, Ammonium, and Rubidium Salts of 1,3-Indanedione-2-sulfonic Acid

Symbol	$C_9H_5O_5SK$			$C_9H_5O_5SNH_4$			$C_9H_5O_5SRb$		
	φ	ρ	No. of meas.	φ	ρ	No. of meas.	φ	ρ	No. of meas.
100	$90^\circ 3' \pm 3'$	$90^\circ 00' \pm 2'$	14	$90^\circ 00' \pm 2'$	$90^\circ 00' \pm 2'$	10	$90^\circ 00' \pm 2'$	$89^\circ 57' \pm 2'$	20
201	$90^\circ 2' \pm 3'$	$56^\circ 6' \pm 9'$	14	—	—	—	$90^\circ 00' \pm 2'$	$55^\circ 28' \pm 4'$	20
201	$90^\circ 00' \pm 3'$	$53^\circ 57' \pm 6'$	14	$90^\circ 00' \pm 2'$	$53^\circ 00' \pm 4'$	10	$90^\circ 00' \pm 2'$	$53^\circ 6' \pm 4'$	20
001	$90^\circ 00' \pm 3'$	$3^\circ 15' \pm 5'$	14	$90^\circ 00' \pm 2'$	$3^\circ 45' \pm 3'$	10	$90^\circ 00' \pm 2'$	$3^\circ 32' \pm 5'$	20
110	$27^\circ 23' \pm 4'$	$90^\circ 00' \pm 2'$	14	$27^\circ 39' \pm 4'$	$90^\circ 00' \pm 2'$	10	$27^\circ 22' \pm 3'$	$89^\circ 57' \pm 2'$	20
011	$2^\circ 23' \pm 5'$	$54^\circ 13' \pm 3'$	14	—	—	—	$2^\circ 36' \pm 4'$	$53^\circ 25' \pm 3'$	20

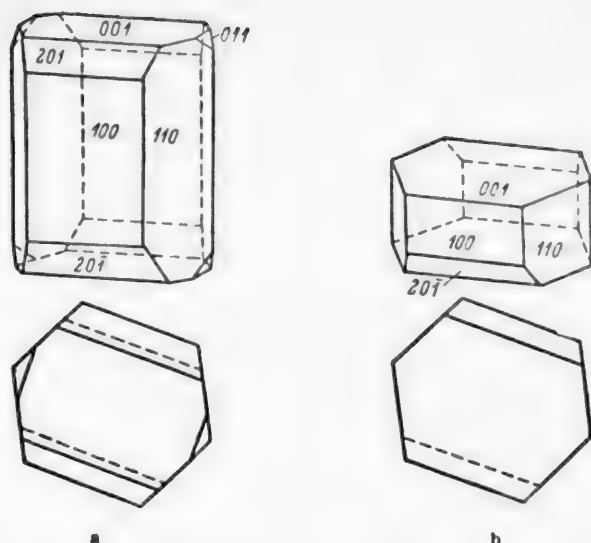


Fig. 4. Crystals of potassium (rubidium) (a) and ammonium (b) salts of 1,3-indanedione-2-sulfonic acid.

Using copper radiation, the unit cell dimensions were determined by powder photographs around [100], [010], and [001]. The following unit cell parameters were calculated from the distances between the planes:

$$a = 11.84 \text{ kX}; b = 6.67 \text{ kX}; c = 14.69 \text{ kX}.$$

On the basis of these data, and using the value of 1.601 g/ml for the specific gravity (d_{20}) of the crystals, we obtained:

1. Ratio of roentgenographic axes:

$$a : b : c = 1.775 : 1 : 2.202.$$

2. Unit cell volume:

$$V = abc \sin \beta = 1148.4 \text{ kX}^3.$$

3. Number of molecules in unit cell:

$$z = \frac{V \cdot d \cdot N}{M} = \frac{1148.4 \cdot 10^{-24} \cdot 1.601 \cdot 0.606 \cdot 10^{24}}{284.22} = 3.92 \sim 4.$$

The translation group was determined with the help of powder photographs around [110], [101], and [011]. The resulting identity periods are set forth in Table 4.

The results indicate that the crystal is based on a primitive translation group.

Potassium, ammonium, and rubidium salts of 1,3-indanedione-2-sulfonic acid $C_9H_5O_5SMe$. Well-developed crystals were obtained by the same procedure as for the sodium salt. Their specific gravities were determined pycnometrically in toluene at 20°. The following values were obtained:

Formula of salt	$C_9H_5O_5SK$	$C_9H_5O_5NH_4$	$C_9H_5O_5SRb$
d_{20}	1.700 g/ml	1.481 g/ml	1.903 g/ml

The crystals were measured with a two-circle, reflecting goniometer. Results are set forth in Table 5.

TABLE 6

Parameters of Unit Cells

Formula	ahX	bhX	chX	β	Volume of unit cell kX^3	No. of molecules in unit cell	Ratio of roentgenographic axes
$C_9H_5O_5SK$	13.96	7.21	10.01	$93^\circ 15' \pm 5'$	1005.9	$3.92 \sim 4$	$1.926 : 1 : 1.388$
$C_9H_5O_5NH_4$	14.40	7.52	9.94	$93^\circ 45' \pm 3'$	1074.0	$4.06 \sim 4$	$1.915 : 1 : 1.322$
$C_9H_5O_5SRb$	14.35	7.45	10.00	$93^\circ 32' \pm 5'$	1067.0	$3.96 \sim 4$	$1.926 : 1 : 1.342$

All of the investigated crystals have a prismatic form and belong to the prismatic class of monoclinic symmetry. The main forms are {100}, {201}, {001}, and {201} pinacoids and {110} and {011} prisms.

Powder diagrams were prepared, using copper radiation, around [100], [010], and [001] for approximate evaluation of the unit cell parameters. Values of a , b , and c calculated from the distances between the layer lines are presented in Table 6. The number of molecules per unit cell was calculated from the unit cell volumes and from the density. The analogous composition and the close similarity in parameters of the unit cell indicate that the three salts are evidently isomorphous.

TABLE 7

Identity Periods of Potassium Salt of
1,3-Indanedione-2-Sulfonic Acid

Direction of rotation	Identity periods (in kX)	
	calc.	found
[110]	15.71	15.63
[101]	17.64	17.70
[011]	12.33	12.40

The ratio of the crystallographic axes was calculated from the coordinates of the (110) and (201) faces. The following values were obtained:



The translation group was determined with the help of additional powder diagrams around [110], [101], and [011]. The identity periods of the potassium salt of 1,3-indanedione-2-sulfonic acid obtained in this way are set forth in Table 7.

TABLE 8

Solubility of Alkali Metal and Ammonium Salts (g per 100 ml) of 1,3-Indanedione-2-Sulfonic Acid in Water and Ethanol at 20°

Solvent	$\text{C}_9\text{H}_6\text{O}_5\text{Li}$	$\text{C}_9\text{H}_6\text{O}_5\text{Na} \cdot 2\text{H}_2\text{O}$	$\text{C}_9\text{H}_6\text{O}_5\text{NH}_4$	$\text{C}_9\text{H}_6\text{O}_5\text{SK}$	$\text{C}_9\text{H}_6\text{O}_5\text{SRb}$
Water	22.91	11.50	4.27	0.822	1.13
Ethanol	0.155	0.097	0.082	0.021	0.021

These results indicate that the crystal is based on a primitive translation group. In view of the complete analogy between the salts investigated, the foregoing observations may also apply to the ammonium and rubidium salts.

The solubilities of the salts were also determined in water and alcohol at 20° (Table 8).

The solubility decreases with increasing radius of the cation.

SUMMARY

Crystals of the lithium, sodium, potassium, ammonium, and rubidium salts of 1,3-indanedione-2-sulfonic acid were investigated. Determinations were made of the crystal class, the unit cell parameters, the number of molecules in the unit cell, and the solubility in water and ethanol at 20°.

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* Original Russian pagination. See C.B. translation.

ANALOGS OF PHTHALOCYANINE

SYNTHESIS AND STUDY OF PROPERTIES

V. F. Borodkin

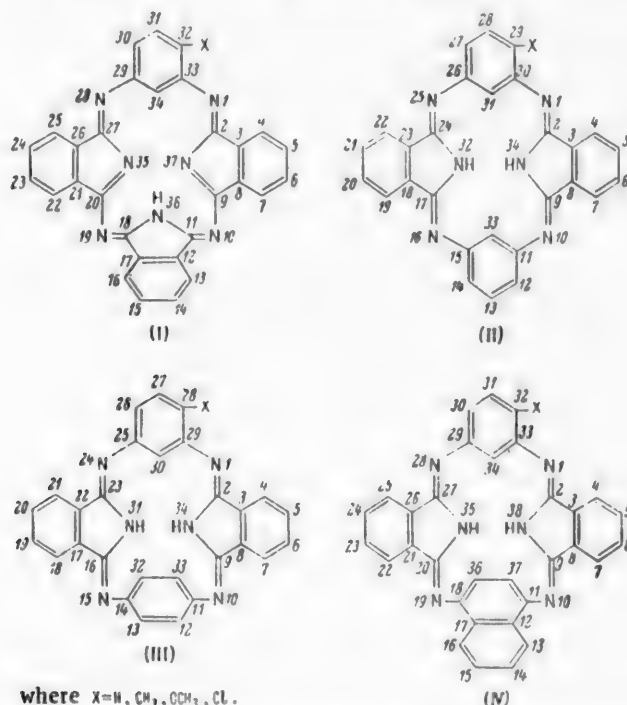
Ivanovo Institute of Chemical Technology

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One of the causes of the deep color of phthalocyanine dyes is undoubtedly the closed conjugated tetraazoporphine (porphyrazine) system, which is the basis of these dyes. Changes in the conjugated chain due to rupture and shortening must lead to a shift of the absorption spectrum into the region of shorter waves, i.e., to deepening of color. On the other hand, destruction of the molecular symmetry must result in lower stability. Interest was therefore attached to a study of the macrocycles whose formulas are given here.



They resemble phthalocyanine in structure, but in place of one or two isoindole nuclei they contain the same number of benzene rings (I, II, III) or one benzene ring and a naphthalene nucleus (IV). The benzene ring also contains various substituents. Replacement of the isoindole nucleus by the benzene ring markedly affects the color of the compound and its stability. Macrorings are much more deeply colored (violet-red and yellow) than phthalocyanine, and they are less resistant to chemical reagents. This is due to replacement of the isoindole nucleus by a benzene ring, which upsets the closed chain of conjugation which characterizes phthalocyanine. The chain undergoes rupture and contraction.

In macrorings with one benzene ring in a system with 1,3-carbon atoms (I), the chain of conjugation is broken but retains an adequate length; such compounds are therefore red-violet. Macrocycles become unstable when they lose their symmetrical structure. They break down in concentrated sulfuric acid. The structure of macrocycles containing a hydrogen or a methyl in place of X has been described in the literature [1]. Substituents

In the benzene ring of macrocycles influence the absorption spectrum, shifting the absorption maximum in the direction of longer waves.

X	λ_{\max} , m μ (in chlorobenzene)
Hydrogen	510
Chlorine	520
Methyl	540

In macrocycles with two benzene rings (II), the conjugated chain is still shorter, and the substituents in the benzene ring do not influence the absorption spectrum of macrocycles in the visible region; their color is therefore yellow (λ_{\max} 360 m μ in methyl alcohol). The structure of macrocycles of this type, containing pyridine, benzene, toluene, or naphthalene rings, has been described in the literature [2,3]. These macrocycles have a symmetrical structure and, therefore, resist the action of chemical reagents.

Macrocycles with one benzene nucleus in a ring of 1,4-carbon atoms (III) also have a yellow color (λ_{\max} 370 m μ in chlorobenzene). This is possibly due to the benzene ring not being in the same plane as the remainder of the molecule and not participating in the conjugation.

Macrocycles with a naphthalene nucleus entering the system at the 1,4-carbon atoms (IV) have an absorption maximum in the near-ultraviolet. Analogous compounds containing a benzene ring (III) have their maximum in the longer-wave region. The absorption maximum depends to some extent on the nature of the substituent.

X	λ_{\max} , m μ (in methanol)
Hydrogen	350
Chlorine	340
Methyl	330
Methoxyl	365

Macrocycles (II, III, IV) are soluble in concentrated sulfuric acid, and insoluble in hydrochloric and other dilute mineral acids, but their yellow color changes to red. The color is restored when the acid solution is made alkaline. These color changes are probably associated with formation of onium salts. The macrocycles are readily soluble in organic solvents on heating, and they are resistant to the action of alkalies. Macrocycles with a naphthalene nucleus (IV) are hydrolyzed when heated in dilute mineral acids.

It should be noted that the nomenclature of the compounds in question has not been fully worked out. Trivial names of compounds proposed by Linstead [1-3], which we used for convenience [4], are unsatisfactory. Such names do not reflect the structure of the macrocycle and the relative positions of the individual rings and heteroatoms. For example, compound (I, X = H) is named triisindole-benzene macrocycle.

In our opinion, the compounds should be given a rational nomenclature with indication of the number of heteroatoms in the large cyclic system, and of the nature and relative position of the other nuclei entering into the macrocycle. On this basis, compound (I, X = H) might be called tetraazacyclo-1,3-phenylenetriisindoline. However, it might be more expedient to name new compounds on the basis of the projected Russian organic nomenclature [5], although this has not yet been generally accepted. We therefore feel constrained in the experimental portion to name the macrocycles on the basis of the Ring Index [6], even though these names are very much less specific than those of the scientific nomenclature of the Russian project. Below we give the rational and scientific names (see A. P. Terent'ev et al. [5]) of the phthalocyanine analogs that we synthesized.

Rational Nomenclature of Synthesized Macrocycles

1. Cyclo-1,3-phenylenetriisindoline (I, X = H)
2. 4-Methylcyclo-1,3-phenylenetriisindoline (I, X = CH₃)
3. 4-Chlorocyclo-1,3-phenylenetriisindoline (I, X = Cl)
4. Cyclo-1,3,1',3'-diphenylenediisindoline (II, X = H)
5. 4-Methylcyclo-1,3,1',3'-diphenylenediisindoline (II, X = CH₃)
6. 4-Methoxycyclo-1,3,1',3'-diphenylenediisindoline (II, X = OCH₃)

7. 4-Chlorocyclo-1,3,1',3'-diphenylenediisoindoline (II, X = Cl)
8. Cyclo-1,3,1',4'-diphenylenediisoindoline (III, X = H)
9. 4-Methylcyclo-1,3,1',4'-diphenylenediisoindoline (III, X = CH₃)
10. 4-Chlorocyclo-1,3,1',4'-diphenylenediisoindoline (III, X = Cl)
11. 4-Methoxycyclo-1,3,1',4'-diphenylenediisoindoline (III, X = OCH₃)
12. Cyclo-1,3-phenylene-1',4'-naphthylenediisoindoline (IV, X = H)
13. 4-Methylcyclo-1,3-phenylene-1',4'-naphthylenediisoindoline (IV, X = CH₃)
14. 4-Chlorocyclo-1,3-phenylene-1',4'-naphthylenediisoindoline (IV, X = Cl)
15. 4-Methoxycyclo-1,4-phenylene-1',4'-naphthylenediisoindoline (IV, X = OCH₃)

Scientific Nomenclature of the Synthesized Macrocycles on the Basis of the Projected Russian Organic Nomenclature

1. 1,10,19,28,35,36,37-Heptaazaocyclo-[3-8,12,17,21-26]-heptatriacontene-2,11,18,20,27-tetraarene-4,13,22,30,30 (I, X = H).
2. 32-Methyl-1,10,19,28,35,36,37-heptaazaocyclo-[3-8,12-17,21-26]-heptatriacontene-2,11,18,20,27-tetraarene-4,13,22,30 (I, X = CH₃).
3. 32-Chloro-1,10,19,28,35,36,37-heptaazaocyclo-[3-8,12-17,21-26]-heptatriacontene-2,11,18,20,27-tetraarene-4,13,22,30 (I, X = Cl).
4. 1,10,16,25,32,34-Hexaazaheptacyclo-[3-8,18-23]-tetratriacontene-2,9,17,24-tetraarene-4,12,19,27 (II, X = H).
5. 29-Methyl-1,10,16,25,32,34-hexaazaheptacyclo-[3-8,18-23]-tetratriacontene-2,9,17,24-tetraarene-4,12,19,27 (II, X = CH₃).
6. 29-Methoxy-1,10,16,25,32,34-hexaazaheptacyclo-[3-8,18-23]-tetratriacontene-2,9,17,24-tetraarene-4,12,19,27 (II, X = OCH₃).
7. 29-Chloro-1,10,16,25,32,34-hexaazaheptacyclo-[3-8,18-23]-tetratriacontene-2,9,17,24-tetraarene-4,12,19,27 (II, X = Cl).
8. 1,10,15,24,31,34-Hexaazaheptacyclo-[3-8,17-22]-tetratriacontene-2,9,16,23-tetraarene-4,12,18,26 (III, X = H).
9. 28-Methyl-1,10,15,24,31,34-hexaazaheptacyclo-[3-8,17-22]-tetratriacontene-2,9,16,23-tetraarene-4,12,18,26 (III, X = CH₃).
10. 28-Chloro-1,10,15,24,31,34-hexaazaheptacyclo-[3-8,17-22]-tetratriacontene-2,9,16,23-tetraarene-4,12,18,26 (III, X = Cl).
11. 28-Methoxy-1,10,15,24,31,34-hexaazaheptacyclo-[3-8,17-22]-tetratriacontene-2,9,16,23-tetraarene-4,12,18,26 (III, X = OCH₃).
12. 1,10,19,28,35,38-Hexaazaocyclo-[3-8,12-17,21-26]-octatriacontene-2,9,20,27-pentaarene-4,13,22,30,37 (IV, X = H).
13. 32-Methyl-1,10,19,28,35,38-hexaazaocyclo-[3-8,12-17,21-26]-octatriacontene-2,9,20,27-pentaarene-4,13,22,30,37 (IV, X = CH₃).
14. 32-Chloro-1,10,19,28,35,38-hexaazaocyclo-[3-8,12-17,21-26]-octatriacontene-2,9,20,27-pentaarene-4,13,22,30,37 (IV, X = Cl).
15. 32-Methoxy-1,10,19,28,35,38-hexaazaocyclo-[3-8,12-17,21-26]-octatriacontene-2,9,20,27-pentaarene-4,13,22,30,37 (IV, X = OCH₃).

EXPERIMENTAL

(With participation of students V. I. Erikhov, M. I. Sokorina, and A. L. Smirnova)

Macrocycles were synthesized by the following procedure. Butyl alcohol was charged into a flask fitted with reflux condenser and stirrer. Equimolar quantities of 1,3-di-(1-imino-3-isoindolinyldeneamino)-benzene (or its substituted derivatives) and 1,3-diiminoisoindoline (or 1,3- or 1,4-phenylenediamine or 1,4-naphthylenediamine) were then dissolved. The solution was boiled until ammonia ceased to come off. The precipitate was filtered and washed with hot methanol or crystallized from suitable solvents until the melting point was unchanged.

7,14,21,27-Tetraaza-22,26-phenylenetriisindoline (I, X = H). Prepared from 36.4 g of 1,3-di-(1-imino-3-isindolinylideneamino)-benzene and 14.5 g of 1,3-diiminoisindoline in 250 ml of butyl alcohol with heating for 10 hr. Yield 70%. M.p. 330-332°. The literature [1] gives m.p. 328-330°. Dark claret needles, insoluble in methanol, ethanol, and acetone; soluble in aromatic hydrocarbons (benzene, toluene, xylene, and nitrobenzene); soluble with later decomposition in concentrated sulfuric and hydrochloric acids.

25-Methyl-7,14,21,27-tetraaza-22,26-phenylenetriisindoline (I, X = CH₃). Prepared from 37.6 g of 2,4-di-(1-imino-3-isindolinylideneamino)-toluene and 14.5 g of diiminoisindoline with heating in 250 ml of butyl alcohol for 10 hr. Yield 72%, m.p. 280°. The literature [1] gives m.p. 285°. Dark claret needles, stable toward alkalis. Soluble in concentrated mineral acids (followed by decomposition), readily soluble in aromatic hydrocarbons (benzene, toluene, xylene, and nitrobenzene) on heating.

25-Chloro-7,14,21,27-tetraaza-22,26-phenylenetriisindoline (I, X = Cl). Prepared from 28 g of 1,3-di-(1-imino-3-isindolinylideneamino)-chlorobenzene and 10.5 g of diiminoisindoline in 300 ml of butyl alcohol with heating for 2 hr. Yield 50%, m.p. 310° (from nitrobenzene).

Found %: C 70.94; H 3.67; N 18.42; Cl 7.20. C₃₀H₁₆N₇Cl. Calculated %: C 70.65; H 3.16; N 19.23; Cl 6.97.

Small, dark-colored, fine needles. Stable toward alkalis. Decomposes in concentrated mineral acids. Soluble in benzene, toluene, and nitrobenzene.

7,13,20,26-Tetraaza-8,12,21,25-diphenylenediisindoline (II, X = H). Prepared from 7.3 g of 1,3-di-(1-imino-3-isindolinylideneamino)-benzene and 2.2 g of m-phenylenediamine with heating in 25 ml of butyl alcohol for 25 hr. Yield 89%. M.p. 363.8-364.2°. The literature [2] gives m.p. 353° (from nitrobenzene).

Found %: C 75.86; H 4.51; N 19.96. C₂₈H₁₈N₆. Calculated %: C 76.54; H 4.12; N 19.34.

24-Methyl-7,13,20,26-tetraaza-8,12,21,25-diphenylenediisindoline (II, X = CH₃). Prepared from 7.3 g of 1,3-di-(1-imino-3-isindolinylideneamino)-benzene and 2.4 g of m-toluylenediamine with heating in butyl alcohol for 24 hr. Yield 47%. M.p. 305.4-306.5°.

Found %: C 76.21; H 5.02; N 18.17. C₂₉H₂₀N₆. Calculated %: C 76.96; H 4.46; N 18.58.

24-Methoxy-7,13,20,26-tetraaza-8,12,21,25-diphenylenediisindoline (II, X = OCH₃). Prepared from 7.3 g of 1,3-di-(1-imino-3-isindolinylideneamino)-benzene and 6.7 g of diaminoanisole sulfate with heating in butyl alcohol for 25 hr. The product was brought down by methanol. Yield 52%. M.p. 33.3-36°.

Found %: C 75.03; H 4.82; N 17.89. C₂₉H₂₀ON₆. Calculated %: C 74.16; H 4.31; N 17.96.

24-Chloro-7,13,20,26-tetraaza-8,12,21,25-diphenylenediisindoline (II, X = Cl). Prepared from 7.9 g of 1,3-di-(1-imino-3-isindolinylideneamino)-benzene and 2.8 g of 2,4-diaminobenzene with heating in butyl alcohol for 30 hr. Yield 32%. M.p. 339-340° (from benzene).

Found %: C 71.47; H 4.47; N 17.31. C₂₈H₁₇N₆Cl. Calculated %: C 71.11; H 3.64; N 17.78.

7,12,19,25-Tetraaza-8,11-20,24-diphenylenediisindoline (III, X = H). Prepared from 3.7 g of 1,3-di-(1-imino-3-isindolinylideneamino)-benzene and 1.2 g of p-phenylenediamine. Yield 72%. M.p. 267.5-268°.

Found %: C 76.37; H 3.76; N 18.72. M 440.2. C₂₈H₁₈N₆. Calculated %: C 76.71; H 4.11; N 19.18; M 438.

23-Methyl-7,12,19,29,35-tetraaza-8,11,20,24-diphenylenediisindoline (III, X = CH₃). Prepared from 3.8 g of 1,3-di-(1-imino-3-isindolinylideneamino)-toluene and 1.2 g of p-phenylenediamine. Yield 74%. M.p. 295.5-286.5°.

Found %: C 76.62; H 3.98; N 17.78. M 452.6. C₂₉H₂₀N₆. Calculated %: C 76.99; H 4.42; N 18.59; M 452.

23-Chloro-7,12,19,25-tetraaza-8,11,20,24-diphenylenediisindoline (III, X = Cl). Prepared from 3.6 g of 1,3-di-(1-imino-3-isindolinylideneamino)-chlorobenzene and 1.2 g of p-phenylenediamine. Yield 68%. M.p. 293-294°.

Found %: C 73.10; H 3.88; N 17.21. M 473.8. C₂₈H₁₇N₆Cl. Calculated %: C 73.22; H 3.59; N 17.08; M 472.5.

23-Methoxy-7,12,19,25-tetraaza-8,11,20,24-diphenylenediisoindoline (III, X = OCH₃). Prepared from 4.3 g of 1,3-di-(1-imino-3-isoindolinylideneamino)-methoxybenzene and 1.2 g of p-phenylenediamine. Yield 63%. M.p. 315.6-316.6°.

Found %: C 74.23; H 4.85; N 17.30. M 470.2. C₂₉H₂₀ON₆. Calculated %: C 74.34; H 4.31; N 17.93. M 468.

7,14,21,27-Tetraaza-8,13-naphthylene-22,26-phenylenediisoindoline (IV, X = H). Prepared from 3.7 g of 1,3-di-(1-imino-3-isoindolinylideneamino)-benzene and 1.6 g of 1,4-naphthylenediamine in 50 ml of butyl alcohol with heating for 50 hr. M.p. 300-303° (from chlorobenzene).

Found %: C 77.83; H 4.35; N 16.98. M 490. C₃₂H₂₀N₆. Calculated %: C 78.67; H 4.14; N 17.19. M 488.

25-Methyl-7,14,21,27-tetraaza-8,13-naphthylene-22,26-phenylenediisoindoline (IV, X = CH₃). Prepared from 3.8 g of 1,3-di-(1-imino-3-isoindolinylideneamino)-toluene and 1.6 g of 1,4-naphthylenediamine in 60 ml of butyl alcohol with boiling for 32 hr. M.p. 312-313.5° (from methanol).

Found %: C 78.03; H 4.70; N 16.45. M 503. C₃₃H₂₂N₆. Calculated %: C 78.86; H 4.42; N 16.72. M 502.

25-Chloro-7,14,21,27-tetraaza-8,13-naphthylene-22,26-phenylenediisoindoline (IV, X = Cl). Prepared from 3.9 g of 1,3-di-(1-imino-3-isoindolinylideneamino)-chlorobenzene and 1.6 g of 1,4-naphthylenediamine in 60 ml of butyl alcohol with boiling for 40 hr. The product was brought down by methanol. M.p. 270-273° (from methanol).

Found %: C 73.04; H 3.81; N 15.85; Cl 8.92. M 523.3. C₃₂H₁₉N₆Cl. Calculated %: C 73.48; H 3.68; N 16.05; Cl 9.38. M 522.5.

25-Methoxy-7,14,21,27-tetraaza-8,13-naphthylene-22,26-phenylenediisoindoline (IV, X = OCH₃). Prepared from 3.9 g of 1,3-di-(1-imino-3-isoindolinylideneamino)-methoxybenzene and 1.6 g of 1,4-naphthylenediamine in 60 ml of butyl alcohol with boiling for 40 hr. M.p. 205-207° (from toluene).

Found %: C 75.96; H 4.44; N 15.85. M 521. C₃₃H₂₂ON₆. Calculated %: C 76.43; H 4.28; N 16.20. M 518.

SUMMARY

1. Twelve macrocycles (analogs of phthalocyanine), not previously described in the literature, were prepared: 25-chloro-7,14,21,27-tetraaza-22,26-phenylenetriisoindoline; 24-methyl-, 24-methoxy-, and 24-chloro-7,13,20,26-tetraaza-8,12,21,25-diphenylenediisoindoline; 7,12,19,25-tetraaza-8,11,20,24-diphenylenediisoindoline; 23-methyl-, 23-methoxy-, and 23-chloro-7,12,19,25-tetraaza-8,11,20,24-diphenylenediisoindoline; 7,14,21,27-tetraaza-8,13-naphthylene-22,26-phenylenediisoindoline; 25-methyl-, 25-methoxy-, and 25-chloro-7,14,21,27-tetraaza-8,13-naphthylene-22,26-phenylenediisoindoline. Their composition and absorption spectra were determined.

2. It was shown that replacement of one or two isoindole nuclei in phthalocyanine by one or two benzene rings leads to a shift of the absorption maximum into the region of shorter waves. Substituents in the benzene ring have little or no influence on the absorption spectrum.

3. A rational and scientific nomenclature was worked out for the macrocycles synthesized.

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ACID CHLORIDES OF N-DICHLOROPHOSPHINYLALENEIMINOSULFONIC ACIDS

E. S. Levchenko and A. V. Kirsanov

Institute of Organic Chemistry, Academy of Sciences of the UkrSSR

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Preparation of derivatives of iminosulfonic acids was first reported in 1858 by R. Fittig [1], and shortly afterwards by C. Gerhardt [2]. However, in 1869, H. Wichelhaus showed that their results were erroneous [3]. O. Wallach and T. Huth [4] attempted to prepare derivatives of iminosulfonic acids by the action of PCl_5 on arylamides of sulfonic acids, but were only able to establish chlorination of the aromatic nucleus attached to the amido group:



In 1930, I. Braun and K. Weissbach [5] reported the preparation of chlorides of N-ethylalkaneiminosulfonic acids by the action of PCl_5 on ethylamides of n-butane-, isopentane-, and cyclohexanesulfonic acids.



According to Braun and Weissbach, these chlorides are hydrolyzed with very great difficulty, and do not react with phenates and amines, i.e., they lack the properties of acid chlorides of sulfonic acids. Braun and Weissbach did not adduce any evidence at all in support of their structure.

There are no grounds for assuming that chlorides of N-ethylalkaneiminosulfonic acids should not possess the properties of acid chlorides (see below). We therefore made a careful experimental check of the work of Braun and Weissbach [5]. It was found that all of the factual data for reaction of PCl_5 with ethylamides of sulfonic acids presented in the paper were inaccurate. Heating of PCl_5 with the ethylamide of n-butanedisulfonic acid leads to release of PCl_3 and not of POCl_3 (see reaction 1). Heating of PCl_5 with the ethylamide of cyclohexanesulfonic acid leads to release of 71.5% of PCl_3 and only 8.8% of POCl_3 . Hence, reaction (1) only takes place to a very minor extent (if at all), the main reaction being chlorination, as observed by Wallach and Huth [4], and not replacement of oxygen atoms by chlorine. Reaction of PCl_5 with the ethylamide of n-butanedisulfonic acid gives 1.5 moles HCl per mole PCl_5 , indicating the detachment of HCl from the initially formed products of chlorination. The resulting unsaturated compounds can be further chlorinated with facility, and in this way we account for the formation of the tetrachloro derivative of the ethylamide of cyclohexanesulfonic acid (see below).

The main bulk of products of reaction of PCl_5 with ethylamides of n-butane- and cyclohexanesulfonic acids comprises noncrystallizing liquids that distill in vacuo with slight decomposition, and contain a high proportion of phosphorus and nonhydrolyzing chlorine. Only a small quantity of crystalline substances can be isolated from these products, and the crystals are not acid chlorides of N-ethylalkaneiminosulfonic acids. The liquid product to which Braun and Weissbach assigned the structure of the acid chloride of N-ethylbutaneiminosulfonic acid, $\text{n-C}_4\text{H}_9\text{SO(=NC}_2\text{H}_5\text{)Cl}$, contains 2.5% of phosphorus, and is evidently a mixture. There are consequently no grounds for assigning to it a definite structure, particularly in the light of its chemical properties. The crystalline substance to which Braun and Weissbach assigned the structure of the chloride of N-ethylcyclohexaneiminosulfonic acid, $\text{C}_6\text{H}_{11}\text{SO(=NC}_2\text{H}_5\text{)Cl}$, has a sharp melting point which is 2° higher than the melting point of the ethylamide of cyclohexanesulfonic acid, does not give a depression in admixture with the latter, but contains about 4% of chlorine. The chlorine content fell after repeated crystallizations (to 2.7% after five crystallizations), but the crystal form and melting point did not alter. In all probability, this substance is a mixture of the original ethylamide of cyclohexanesulfonic acid and products of its chlorination with which it forms mixed crystals. This would account for the sharp melting point and the absence of a melting point depression in admixture with the ethylamide of cyclohexanesulfonic acid. Moreover, a crystalline substance that separated from the products of

TABLE 1

Acid Chlorides of N-Dichlorophosphinylareneinosulfonic Acids of the Type of $\text{XC}_6\text{H}_4\text{SO}(=\text{NPOCl}_2)\text{Cl}$

X	Yield (%)	Melting point	Appearance and solvent from which crystallized	Empirical formula	Found %	Calculated %
H	100***	—	Viscous liquid	$\text{C}_6\text{H}_5\text{O}_2\text{NSPCL}_3$	Cl 35.89, 35.81equiv 5.10, 5.05	Cl 36.38
<i>o</i> -CH ₃	68	70–71°	Prisms, CCl_4	$\text{C}_7\text{H}_7\text{O}_2\text{NSPCL}_3$	Cl 34.52, 34.29, <i>M</i> 326, 312equiv 4.96, 4.97	Cl 34.74, <i>M</i> 307
<i>p</i> -CH ₃	67	53–54	Plates, ligroine	$\text{C}_7\text{H}_7\text{O}_2\text{NSPCL}_3$	Cl 35.11, 35.13, <i>M</i> 318, 321equiv 4.92, 4.91	Cl 34.74, <i>M</i> 307
<i>o</i> -Cl	40	74–76	The same	$\text{C}_6\text{H}_4\text{O}_2\text{NSPCL}_4$	Cl 32.31, 32.35, ****equiv 4.92, 4.91	Cl 32.56****
<i>p</i> -Cl	69	71–72	The same	$\text{C}_6\text{H}_4\text{O}_2\text{NSPCL}_4$	Cl 43.64, 43.75; <i>P</i> 9.55, 9.57, <i>M</i> 328, 307equiv 4.94, 5.06	Cl 43.45; <i>P</i> 9.47, <i>M</i> 327
<i>p</i> -Br	95	79–80	Plates, hexane	$\text{C}_6\text{H}_4\text{O}_2\text{NSPCL}_3\text{Br}$	Cl 28.51, 28.40equiv 4.89, 4.92	Cl 28.67
<i>p</i> -F	100***	—	Viscous liquid	$\text{C}_6\text{H}_4\text{O}_2\text{NSPFCL}_3$	Cl 33.98, 33.89equiv 4.99, 4.96	Cl 34.20
<i>p</i> -CH ₃ O	64	38–40	Plates, ligroine	$\text{C}_7\text{H}_7\text{O}_3\text{NSPCL}_3$	Cl 32.82, 32.46equiv 4.92, 4.82	Cl 33.02
<i>m</i> -CF ₃	100***	—	Viscous liquid	$\text{C}_7\text{H}_4\text{O}_3\text{NSPF}_3\text{Cl}_3$	Cl 29.20, 29.05equiv 5.02, 5.04	Cl 29.51

*Equiv. after hydrolysis. Molecular weight cryoscopically in benzene.

**Equiv. after hydrolysis of 5.00 calculated for all compounds

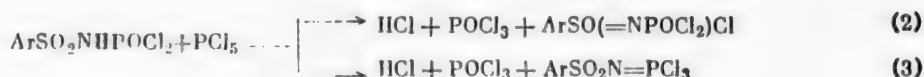
***Crude product.

****Hydrolyzable chlorine.

reaction of PCl_5 with the ethylamide of cyclohexanesulfonic acid corresponded in composition to a tetrachloro derivative of the ethylamide of cyclohexanesulfonic acid. The liquid products of reaction of PCl_5 with the ethylamide of cyclohexanesulfonic acid contain a high proportion of phosphorus. Far-reaching chlorination is accordingly the main process when PCl_5 acts on the ethylamides of *n*-butane- and cyclohexanesulfonic acids, and this explains the formation of PCl_3 and the presence of unchanged starting substance after reaction. Formation of phosphorus-containing compounds of unknown structure proceeds at the same time as chlorination.

It has thus been shown that the compounds obtained by Braun and Weissbach by the action of PCl_5 on ethylamides of sulfonic acids are not (judging by their composition and chemical properties) acid chlorides of *N*-ethyl-, *n*-butane-, and *N*-ethylcyclohexaniminosulfonic acids. Consequently, not a single acid chloride of an iminosulfonic acid has been prepared up to the present time.

Reaction of PCl_5 with the diacid chlorides of arylsulfonamidophosphoric acids might be expected to yield either acid chlorides of *N*-dichlorophosphinylareneiminosulfonic acids [reaction (2)] or trichlorophosphazosulfonyls [reaction (3)].



Experiments showed that diacid chlorides of arylsulfonamidophosphoric acids in which the aryls contain electronegative substituents react with PCl_5 according to Eq. (3) [6], but in all cases the reaction is accompanied by formation of noncrystallizing secondary products from which pure substances have not so far been isolated (see below). In reaction of PCl_5 with diacid chlorides of arylsulfonamidophosphoric acids whose aryls do not contain electronegative substituents, one mole of HCl and one mole of POCl_3 are released and the acid chlorides of *N*-dichlorophosphinylareneiminosulfonic acids are formed in good yields in accordance with Eq. (2). Their structure is confirmed by elementary analysis, by determinations of their molecular weights and chemical properties, and also by the composition and properties of their derivatives, namely the phenyl esters of *N*-diphenyloxyphosphinylareneiminosulfonic acids.

Formation of acid chlorides of *N*-dichlorophosphinylareneiminosulfonic acids by the action of PCl_5 on diacid chlorides of arylsulfonamidophosphoric acids opens up a route to the preparation of diverse derivatives of iminosulfonic acids, and to the study of the properties of this new class of compounds. Acid chlorides of *N*-dichlorophosphinylareneiminosulfonic acids of the type $\text{ArSO}(=\text{NPOCl}_2)\text{Cl}$ (Table 1) are colorless, crystalline or liquid substances, insoluble in water, readily soluble in ether, benzene, CCl_4 , dioxane, acetone, and chloroform, sparingly soluble in ligroine, and having a characteristic weak odor resembling that of acid chlorides of arenesulfonic acids. Most of them melt below the corresponding isomeric trichlorophosphazosulfonyls, and the melting points of their mixtures with the latter are sharply depressed.

Chemically, the acid chlorides of *N*-dichlorophosphinylareneiminosulfonic acids are typical acid chlorides and exhibit all the reactions of acid chlorides of arenesulfonic acids and of diacid chlorides of arylsulfonamidophosphoric acids, but differ from the latter in lacking the properties of acids [7]. At room temperature they are slowly hydrolyzed by water (at approximately the same rate as acid chlorides of arenesulfonic acids, and very much more slowly than the corresponding isomeric trichlorophosphazosulfonyls). They are rapidly hydrolyzed by boiling water.



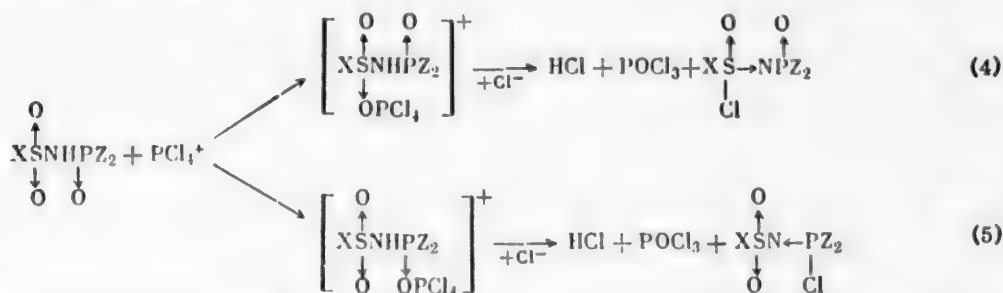
Acid chlorides of *N*-dichlorophosphinylareneiminosulfonic acids easily enter into reaction with alcohols, phenols, ammonia, amines, alkoxides, phenoxides, and other compounds containing active atoms of hydrogen or metals. Treatment with sodium phenoxide or *p*-nitrophenoxide converts them in good yields into aryl esters of *N*-diaroxyposphinylareneiminosulfonic acids (Table 2).



Aryl esters of *N*-diaroxyposphinylareneiminosulfonic acids are colorless, crystalline, neutral substances whose chemical properties resemble those of aryl esters of aromatic sulfonic acids and diaryl esters of arylsulfonamidophosphoric acids, although they differ from the latter in not being acidic. They are hydrolyzed with

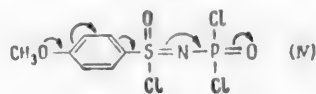
considerably greater difficulty than their isomeric triaroxyphosphazosulfonyls, and in admixture with the latter their melting points are sharply depressed. Drastic saponification with caustic alkalis in aqueous alcoholic solutions gives the diphenyl esters of arylsulfonamidophosphoric acids. This reaction, considered in association with results of determinations of elemental composition and molecular weight and with the method of formation, can be taken as proof of their structure.

Up to now, no cases were known of reaction of PCl_5 with the $>\text{SO}_2$ group in sulfones or sulfonic acid derivatives that could lead to replacement of the oxygen atoms of the $>\text{SO}_2$ group by chlorine atoms. It was therefore of interest to consider the possible causes of formation of acid chlorides of N-dichlorophosphinyliminosulfonic acids by reaction (4). The oxygen atoms bound to sulfur and phosphorus atoms in molecules of the type of $\text{XSO}_2\text{NHPZ}_2$ can react with PCl_5 .



Reaction (4) can take place if the electronic density at the oxygen atom attached to the sulfur atom is greater than that at the oxygen atom attached to the phosphorus atom — and conversely. Therefore, factors that promote an increased electronic density of the oxygen of the $\text{S} \rightarrow \text{O}$ group must promote reaction (4), while factors that promote an increased electronic density of the oxygen of the $\text{P} \rightarrow \text{O}$ group must promote reaction (5). Hence, the less electronegative is group X, the greater the probability that reaction (4) will take place; on the other hand, the less electronegative are the Z groups, the greater the probability that reaction (5) will take place. The most favorable conditions for formation of acid chlorides of iminosulfonic acids are created when group X has minimum electronegativity [so promoting reaction (4)], and groups Z have maximum electronegativity [which suppresses reaction (5)]. The second step of the reaction — cleavage of the addition product by the action of HCl — must proceed the more easily the greater the polarization of the $\text{S} \rightarrow \text{O}$ bonds and, in turn, of the $\text{P} \rightarrow \text{O}$ bonds. Consequently, the nature of the X and Z groups affects the second steps of the reaction in the same direction as they affect the first steps, since increased electronegativity of X and Z hinders polarization of the $\text{S} \rightarrow \text{O}$ and $\text{P} \rightarrow \text{O}$ bonds, respectively.

Since the probability of the reaction proceeding in one direction or the other depends not only on the possibility of formation of intermediate products, but also on the "gainfulness" of the end product, consideration should also be given to the influence of the nature of the X and Z groups on the stability of the final reaction products. The nature of Z evidently has little influence on the stability of the end products, but that of X has a great influence. If X groups are first-order substituents in the benzene ring in the ortho- and para-positions, then the bonds in the acyclic part of the conjugated system in the resulting acid chloride of the N-dichlorophosphinyl areneiminosulfonic acid may become equivalent, with consequent stabilization of the molecule. For example:



The presence of second-order substituents suppresses the possibility of bond equivalence. Consequently, the presence in the benzene ring of group X of electropositive substituents favors reaction (4) not only because it renders the whole of group X less electronegative, but also because it makes the end product more gainful. The influence of substituents in the benzene ring is transmitted by mesomeric and inductive effects, since ortho-, meta- and para-nitro derivatives mainly react according to (5) with formation of phosphazo compounds. However, the mesomeric effect plays a much bigger part than the inductive effect, since the acid chloride of m-trifluoromethylphenylsulfonamidophosphoric acid reacts mainly according to (5), i.e., in this case the $\text{m}-\text{CF}_3\text{C}_6\text{H}_4$ group is not sufficiently electronegative to enable reaction (4) to take place.

TABLE 2
Aryl Esters of N-Diaroxophosphinylareneiminosulfonic Acids of the Type of $\text{XC}_6\text{H}_4\text{SO}[\text{=NPO}(\text{OC}_6\text{H}_4)_2](\text{OC}_6\text{H}_4\text{Y})$

X	Y	Yield (%)	Melting point	Outward appearance, solvent from which crystallized	Empirical formula	Found %	Calc. %	Solubilities*				
								ethanol	acetone	benzene	CCl ₄	ether
H	H	73	101—102°	Prisms, ethanol	$\text{C}_{24}\text{H}_{20}\text{O}_5\text{NSP}$	N 3.02, 3.04, 3.06 M 470**	N 3.01, 3.04, 3.06 M 465	—	—	—	—	—
p-CH ₃	H	57	61—62	Prisms, CCl ₄	$\text{C}_{25}\text{H}_{21}\text{O}_5\text{NSP}$	P 6.17, 6.05	P 6.47	—	—	—	—	—
p-Cl	H	66	95—97	Fine needles, methanol	$\text{C}_{24}\text{H}_{19}\text{O}_5\text{NSP}$	Cl 7.31, 7.27	Cl 7.40	—	—	—	—	—
p-Br	H	61	82—83	Prisms, methanol or ethanol	$\text{C}_{24}\text{H}_{19}\text{O}_5\text{NSPBr}$	Br 14.94, 15.08	Br 14.70	—	—	—	—	—
p-F	H	83	92—93	Prisms, ethanol	$\text{C}_{24}\text{H}_{19}\text{O}_5\text{NSPF}$	P 6.56, 6.13	P 6.41	—	—	—	—	—
o-CH ₃	p-NO ₂	61	131—132	The same	$\text{C}_{25}\text{H}_{19}\text{O}_5\text{N}_2\text{SP}$	N 8.92, 8.79	N 9.12	—	—	—	—	—
o-Cl	p-NO ₂	44	133—134	The same	$\text{C}_{24}\text{H}_{18}\text{O}_5\text{N}_2\text{SPCl}$	N 8.40, 8.50	N 8.82	—	—	—	—	—
p-CH ₃ O	p-NO ₂	87	119—120	The same	$\text{C}_{25}\text{H}_{19}\text{O}_6\text{N}_2\text{SP}$	N 8.93, 8.76	N 8.83	—	—	—	—	—
p-CF ₃	p-NO ₂	55	141—142	Plates, benzene	$\text{C}_{25}\text{H}_{18}\text{O}_6\text{N}_2\text{SPF}_3$	N 8.58, 8.61	N 8.68	—	—	—	—	—

* + denotes easily soluble at boiling point; — denotes sparingly soluble at the boil; = denotes insoluble at the boil.

** Rast determination.

On the basis of the foregoing considerations we can infer that lowering of the electronegativity of group X speeds up the first and second steps of reaction (4) and makes the structure of the end product more gainful, while lowering of the electronegativity of groups Z speeds up the first and second steps of reaction (5) and thereby counteracts reaction (4). The experimental results fully confirm these conclusions. In Table 3 are set forth examples of all of the four theoretically possible combinations of groups X and Z in compounds of the type of $\text{XSO}_2\text{NHPOZ}_2$.

We see from the table that reaction (4) only takes place when groups Z are of such a nature that they suppress reaction (5), and groups X are of such a nature that they promote both steps of reaction (4) and the gainfulness of the end product. It is unlikely, however, that diacid chlorides of arylsulfonamidophosphoric acids with electronegative groups X would react only according to reaction (5), and that those with electropositive groups X would react only according to reaction (4). The reaction probably goes in both directions, but only the product of the main direction can be isolated in the pure state, since acid chlorides of N-dichlorophosphinylareneiminosulfonic acids and the corresponding isomeric trichlorophosphazosulfonaryls possess very similar physical and chemical properties and give low-melting eutectic mixtures. It is highly probable that such mixtures are non-crystallizing secondary products of reaction of PCl_5 with acid chlorides of arylsulfonamidophosphoric acids containing both electropositive and electronegative aryl groups. The above theoretical conclusions not only account for the formation of acid chlorides of N-dichlorophosphinylareneiminosulfonic acids by the action of PCl_5 , but also point to routes for synthesis of derivatives of iminosulfonic acids by other methods.

EXPERIMENTAL

Acid chlorides of N-dichlorophosphinyl-iminosulfonic acids (Table 1). A mixture of 0.1 mole of diacid chloride of arylsulfonamidophosphoric acid, 0.103 mole of PCl_5 , and 20 ml of CCl_4 was refluxed on an oil bath at 90° until HCl ceased to come off. Solvent and POCl_3 were distilled off in vacuo.

TABLE 3

Direction of Reaction $\text{XSO}_2\text{NHPOZ}_2 + \text{PCl}_5 \rightarrow \text{XSO} (= \text{NPOZ}_2)\text{Cl}$ or $\text{XSO}_2 = \text{NPZ}_2\text{Cl}$

Group X	Group Z	Direction of reaction
C_6H_5 , p- ClC_6H_4 (relatively* electro-negative)	OC_6H_5 (relatively electropositive)	(III), $\text{ArSO}_2\text{N} = \text{P}(\text{OC}_6\text{H}_5)\text{Cl}$ [6]
C_6H_5 , o- and p- $\text{CH}_3\text{C}_6\text{H}_4$, p- $\text{CH}_3\text{OC}_6\text{H}_4$, p- ClC_6H_4 , p- BrC_6H_4 , p- FC_6H_4 , and m- $\text{CF}_3\text{C}_6\text{H}_4$ (relative-ly electropositive)	Cl (relatively electronegative)	(II), $\text{ArSO} (= \text{NPOCl}_2)\text{Cl}$
o-, m-, and p- $\text{NO}_2\text{C}_6\text{H}_4$ (relatively electronegative)	OC_6H_5 (relatively electropositive)	(III), $\text{ArSO}_2\text{N} = \text{P}(\text{OC}_6\text{H}_5)_2\text{Cl}$ [6]
o-, m-, and p- $\text{NO}_2\text{C}_6\text{H}_4$ and p- $\text{C}_6\text{H}_5\text{OSO}_2\text{C}_6\text{H}_4$ (relatively electronegative)	Cl (relatively electronegative)	(III), $\text{ArSO}_2\text{N} = \text{PCl}_3$ [6]

*For the given reaction.

The residual yellow oil crystallized on cooling in the majority of cases. Quantitative yields. Experiments in which the amount of HCl and POCl_3 was determined were performed without a solvent. Yield of HCl about 90%, yield of POCl_3 80-95%.

Aryl esters of N-dichlorophosphinylareneiminosulfonic acids (Table 2). A mixture of 0.01 mole of acid chloride of N-dichlorophosphinylareneiminosulfonic acid, 0.03 mole of sodium aryloxide, and 50 ml of benzene was refluxed for an hour. The NaCl was filtered off from the hot solution, the filtrate was evaporated to dryness in vacuo, and the ester was crystallized from a suitable solvent.

Hydrolysis of esters. A mixture of 2 ml of 1 N aqueous KOH , 1 ml of water, 2 ml of alcohol, and 0.001 mole of aryl ester of N-diaroxyphosphinylareneiminosulfonic acid was refluxed until the whole of the ester had dissolved (1.5-5 hr), the alcohol was taken off in vacuo, and 1.5 ml of 1 N HCl solution was added to the solution. The diaryl esters of arylsulfonamidophosphoric acids came down and were suction-filtered, recrystallized, and identified by mixed melting point test. Yields 80-95%.

Reaction of PCl_5 with ethylamide of n-butanesulfonic acid [5]. The reaction led to release of 1.5 moles of HCl per mole of PCl_5 . After the reaction had been completed, the PCl_3 was taken off in vacuo at 100° in an apparatus fitted with a receiver cooled to -70° . From the distillate was isolated 45.5% of PCl_3 (calculated on the PCl_5). POCl_3 was not found in the distillate. The residue was a dark, mobile liquid (13 g). It was distilled in vacuo, and the greater part (8.4 g) came over at $134-136^\circ$ (0.15 mm) as a transparent, nearly colorless, but very rapidly darkening liquid containing about 2.5% of phosphorus, which was not removed on subsequent distillations. Small lower and higher fractions also contained phosphorus.

Reaction of PCl_5 with ethylamide of cyclohexanesulfonic acid was carried out under the conditions described by Braun and Weissbach [5]. After completion of the reaction the chlorides of phosphorus were removed in vacuo at 100° (receiver cooled to -70°). From the distillate was isolated 71.5% of PCl_3 and 8.8% of POCl_3 (calculated on the PCl_5). The residue after removal of the phosphorus chlorides was a dark, viscous mass (26 g from 0.1 mole of ethylamide of cyclohexanesulfonic acid), which partly crystallized on cooling. The product distilled in vacuo with partial decomposition. All the fractions contained phosphorus and chlorine. The main bulk (13 g) came over at $148-158^\circ$ (0.7 mm). The cooled distillate changed into a semiliquid crystalline mass. The crystals were suction-filtered and washed with ether. Yield 4.6 g (from 0.1 mole of starting substance); recrystallization from hexane gave colorless plates with m.p. $73-74^\circ$; the product contained about 4% of chlorine (not hydrolyzable), and did not give a depression of melting point in admixture with the ethylamide of cyclohexanesulfonic acid. The appearance and melting point remained unchanged after a further four recrystallizations, but the chlorine content fell to 2.7%.

In another experiment the phosphorus chlorides were distilled off from the reaction product (from 0.1 mole of starting substance), which was then mixed with 10 ml of ligroine. Crystals came down and were collected, washed with 5 ml of ether, and recrystallized from ligroine. Yield 5 g, m.p. 147-148° (decomp.). In composition the substance corresponds to the tetrachloro derivative of the ethylamide of cyclohexanesulfonic acid.

Found %: Cl 42.48; 42.49; S 9.39, 9.27. $C_6H_{13}NSCl_4$. Calculated %: Cl 43.16, S 9.72.

Pyrolysis (140°) or boiling with water led to cleavage of 1 mole of HCl from the tetrachloro derivative, and to formation of a substance which, after recrystallization from ethylene chloride, had m.p. 171-172° (decomp.).

SUMMARY

1. Reaction of PCl_5 with diacid chlorides of arylsulfonamidophosphoric acids whose aryls do not contain negative substituents gave acid chlorides of N-dichlorophosphinylareneiminosulfonic acids. The chemical properties of the products resemble those of sulfonic acid chlorides and diacid chlorides of arylsulfonamidophosphoric acids, but they differ from the latter in being free of acidic properties.

2. Acid chlorides of N-dichlorophosphinylareneiminosulfonic acids react with sodium aryloxides to form aryl ethers of N-diaroxyphosphinylareneiminosulfonic acids.

3. The substances obtained by I. Braun and K. Weissbach on reaction of PCl_5 with ethylamides of n-butane-, isopentane-, and cyclohexanesulfonic acids were wrongly assigned the structure of acid chlorides of n-butane-, isopentane-, and cyclohexane-N-ethyliminosulfonic acids.

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ESTERS OF ARYLSULFONIMIDOPHENYLPHOSPHINIC ACIDS

V. I. Shevchenko and V. T. Stratienko

Dnepropetrovsk Metallurgical Institute

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Phenyldichlorophosphazosulfonyls, easily obtained in good yield by A. V. Kirsanov's phosphazo reaction [1], can serve as starting substances for preparation of various derivatives of arylsulfonimidophosphinic acids. Products of reaction of phenyldichlorophosphazosulfonyls with aniline [2] and ammonia [3] have been described and certain characteristics distinguishing phenyldichlorophosphazosulfonyls from trichlorophosphazosulfonyls have been noted.

In the present work we studied the reactions of phenyldichlorophosphazosulfonyls with sodium alkoxides and phenoxides. Reaction of phenyldichlorophosphazosulfonyls (I) with sodium alkoxides gives (depending on the ratio of reactants), either phenyldialkoxyposphazosulfonyls (dialkyl esters of arylsulfonimidophenylphosphinic acids) (II) or sodium salts of monoalkyl esters of arylsulfonamidophenylphosphinic acids (III).

*Original Russian pagination. See C.B. translation.

TABLE 1

Phenyldialkoxyposphazosulfonyls $\text{ArSO}_2\text{N} = \text{P}(\text{C}_6\text{H}_5)(\text{OAlk})_2$

Prep. No.	Ar	Alk	Yield (%)	Melting point	OAlk found (%)	OAlk calc. (%)	Empirical formula
1	C_6H_5	CH_3	86.3	48°	19.36	19.1	$\text{C}_{14}\text{H}_{16}\text{O}_4\text{NSP}$
2	$o\text{-CH}_3\text{C}_6\text{H}_4$	CH_3	78.7	59	19.18	18.3	$\text{C}_{15}\text{H}_{16}\text{O}_4\text{NSP}$
3	$p\text{-CH}_3\text{C}_6\text{H}_4$	CH_3	76.8	65	18.24	18.3	$\text{C}_{15}\text{H}_{18}\text{O}_4\text{NSP}$
4	$m\text{-C}_{10}\text{H}_7$	CH_3	78.0	79	16.53	16.55	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{NSP}$
5	$\beta\text{-C}_{10}\text{H}_7$	CH_3	84.0	95	16.58	16.55	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{NSP}$
6	$o\text{-NO}_2\text{C}_6\text{H}_4$	CH_3	67.0	49	16.47	16.75	$\text{C}_{14}\text{H}_{15}\text{O}_6\text{N}_2\text{SP}$
7	$m\text{-NO}_2\text{C}_6\text{H}_4$	CH_3	68.1	64	16.66	16.75	$\text{C}_{14}\text{H}_{15}\text{O}_6\text{N}_2\text{SP}$
8	C_6H_5	C_2H_5	80.1	Liquid	25.4	25.5	$\text{C}_{16}\text{H}_{20}\text{O}_4\text{NSP}$
9	$o\text{-CH}_3\text{C}_6\text{H}_4$	C_2H_5	78.7	100–102	24.50	24.52	$\text{C}_{17}\text{H}_{22}\text{O}_4\text{NSP}$
10	$p\text{-CH}_3\text{C}_6\text{H}_4$	C_2H_5	80.4	Liquid	24.16	24.52	$\text{C}_{17}\text{H}_{22}\text{O}_4\text{NSP}$
11	$m\text{-C}_{10}\text{H}_7$	C_2H_5	87.9	85	22.28	22.33	$\text{C}_{20}\text{H}_{22}\text{O}_4\text{NSP}$
12	$\beta\text{-C}_{10}\text{H}_7$	C_2H_5	81.0	Liquid	22.21	22.33	$\text{C}_{20}\text{H}_{22}\text{O}_4\text{NSP}$
13	$o\text{-NO}_2\text{C}_6\text{H}_4$	C_2H_5	64.7	Liquid	22.21	22.6	$\text{C}_{16}\text{H}_{19}\text{O}_6\text{N}_2\text{SP}$
14	$m\text{-NO}_2\text{C}_6\text{H}_4$	C_2H_5	62.8	Liquid	22.41	22.6	$\text{C}_{16}\text{H}_{19}\text{O}_6\text{N}_2\text{SP}$

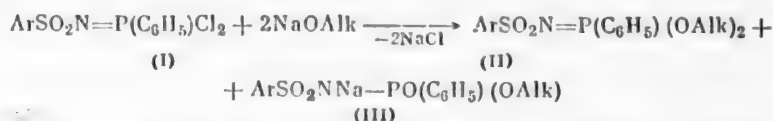
TABLE 2

Monoalkyl Esters of Arylsulfonamidophenylphosphinic Acids $\text{ArSO}_2\text{NHIPO}(\text{C}_6\text{H}_5)(\text{OAlk})$ [by hydrolysis of (II)]

Prep. No.	Ar	Alk	Yield (%)	Melting point	Equiv. found*	Empirical formula
1	$p\text{-CH}_3\text{C}_6\text{H}_4$	CH_3	86.2	156–157°	0.99	$\text{C}_{14}\text{H}_{16}\text{O}_4\text{NSP}$
2	$m\text{-C}_{10}\text{H}_7$	CH_3	97.8	155–157	1.01	$\text{C}_{17}\text{H}_{16}\text{O}_4\text{NSP}$
3	$p\text{-CH}_3\text{C}_6\text{H}_4$	C_2H_5	90.9	167–168	0.93	$\text{C}_{15}\text{H}_{18}\text{O}_4\text{NSP}$
4	$m\text{-NO}_2\text{C}_6\text{H}_4$	C_2H_5	95.4	140–143	0.97	$\text{C}_{14}\text{H}_{15}\text{O}_6\text{N}_2\text{SP}$
5	$\beta\text{-C}_{10}\text{H}_7$	C_2H_5	77.7	195–197	0.99	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{NSP}$

*Calculated equiv.: 1.00.

Phenyldialkoxyposphazosulfonyls (II) are easily obtained, and in good yield, if a benzene solution of phenyldichlorophosphazosulfonyl (I) (Table 1) is added with cooling and stirring to an alcoholic solution of the sodium alkoxide. A secondary product formed in small quantity is the sodium salt of the monoalkyl ester (III).



Phenyldialkoxyposphazosulfonyls (II) are colorless, crystalline substances or viscous, oily liquids, readily soluble in acetone, benzene, hot CCl_4 , and alcohol; insoluble in water, ether, and ligroine; the solids crystallize nicely from alcohol. Chemically, compounds (II) are stable and neutral; they are inert to water and do not react with it even after prolonged heating; they are not appreciably attacked by aqueous solutions of acids and alkalis; however, they are readily hydrolyzed by alcoholic or aqueous alcoholic solutions of alkalis and acids. In an alkaline medium the phenyldialkoxyposphazosulfonyls (II) behave like esters of polybasic mineral acids in losing only one alcohol group with formation of monoalkyl esters of arylsulfonamidophenylphosphinic acids (III) (Table 2). Acidification of aqueous solutions of the sodium salts leads to precipitation of the sparingly water-soluble monoalkyl esters of arylsulfonamidophenylphosphinic acids. In an acid medium (II) are hydrolyzed to arylsulfamides, probably according to the reaction:

TABLE 3

Monoalkyl Esters of Arylsulfonamidophenylphosphinic Acids
 $\text{ArSO}_2\text{NHPO}(\text{C}_6\text{H}_5)(\text{OAlk})$ [directly from (I)]

Prep. No.	Ar	Alk	Yield (%)	Melting point	Found equiv.*	Empirical formula
1	C_6H_5	CH_3	75.0	172–173°	1.03	$\text{C}_{13}\text{H}_{14}\text{O}_4\text{NSP}$
2	$o\text{-CH}_3\text{C}_6\text{H}_4$	CH_3	81.2	166–168	0.98	$\text{C}_{14}\text{H}_{16}\text{O}_4\text{NSP}$
3	$p\text{-CH}_3\text{C}_6\text{H}_4$	CH_3	80.0	156–157	1.00	$\text{C}_{14}\text{H}_{16}\text{O}_4\text{NSP}$
4	$o\text{-NO}_2\text{C}_6\text{H}_4$	CH_3	91.5	161–162	1.03	$\text{C}_{13}\text{H}_{13}\text{O}_6\text{N}_2\text{SP}$
5	$p\text{-NO}_2\text{C}_6\text{H}_4$	CH_3	66.3	175–176	0.99	$\text{C}_{13}\text{H}_{13}\text{O}_6\text{N}_2\text{SP}$
6	$p\text{-ClC}_6\text{H}_4$	CH_3	67.5	165–167	1.05	$\text{C}_{13}\text{H}_{13}\text{O}_4\text{NSPCl}$
7	$\alpha\text{-C}_{10}\text{H}_7$	CH_3	80.6	165–157	1.00	$\text{C}_{17}\text{H}_{16}\text{O}_4\text{NSP}$
8	$\beta\text{-C}_{10}\text{H}_7$	CH_3	71.7	165–166	1.00	$\text{C}_{17}\text{H}_{16}\text{O}_4\text{NSP}$
9	C_6H_5	C_2H_5	96.1	141–142	1.00	$\text{C}_{14}\text{H}_{16}\text{O}_4\text{NSP}$
10	$o\text{-CH}_3\text{C}_6\text{H}_4$	C_2H_5	97.1	156–158	1.02	$\text{C}_{15}\text{H}_{18}\text{O}_4\text{NSP}$
11	$p\text{-CH}_3\text{C}_6\text{H}_4$	C_2H_5	86.7	165–167	0.99	$\text{C}_{15}\text{H}_{18}\text{O}_4\text{NSP}$
12	$p\text{-ClC}_6\text{H}_4$	C_2H_5	86.8	158–160	0.98	$\text{C}_{14}\text{H}_{15}\text{O}_4\text{NSPCl}$
13	$\alpha\text{-C}_{10}\text{H}_7$	C_2H_5	89.3	148–150	0.98	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{NSP}$
14	$\beta\text{-C}_{10}\text{H}_7$	C_2H_5	86.8	195–197	0.99	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{NSP}$
15	C_6H_5	$n\text{-C}_3\text{H}_7$	84.1	110–112	1.01	$\text{C}_{15}\text{H}_{18}\text{O}_4\text{NSP}$
16	$o\text{-CH}_3\text{C}_6\text{H}_4$	$n\text{-C}_3\text{H}_7$	90.9	129–130	0.96	$\text{C}_{16}\text{H}_{20}\text{O}_4\text{NSP}$
17	$p\text{-CH}_3\text{C}_6\text{H}_4$	$n\text{-C}_3\text{H}_7$	97.0	138–140	0.98	$\text{C}_{16}\text{H}_{20}\text{O}_4\text{NSP}$
18	$p\text{-ClC}_6\text{H}_4$	$n\text{-C}_3\text{H}_7$	86.7	130–134	0.97	$\text{C}_{15}\text{H}_{17}\text{O}_4\text{NSPCl}$
19	$\alpha\text{-C}_{10}\text{H}_7$	$n\text{-C}_3\text{H}_7$	93.7	137–139	0.98	$\text{C}_{19}\text{H}_{20}\text{O}_4\text{NSP}$

* Calculated equiv.: 1.00.

TABLE 4

Phenyldiphenoxypyphosphazosulfonyls $\text{ArSO}_2\text{N} = \text{P}(\text{C}_6\text{H}_5)(\text{OC}_6\text{H}_5)_2$

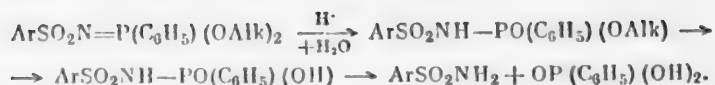
Prep. No.	Ar	Yield (%)	Melting point	Found % N	Calc. % N	Empirical formula
1	C_6H_5	80.6	64–65°	3.08	3.10	$\text{C}_{24}\text{H}_{20}\text{O}_4\text{NSP}$
2	$o\text{-CH}_3\text{C}_6\text{H}_4$	73.8	56–58	3.06	3.02	$\text{C}_{25}\text{H}_{22}\text{O}_4\text{NSP}$
3	$p\text{-CH}_3\text{C}_6\text{H}_4$	82.4	88–89	3.08	3.02	$\text{C}_{25}\text{H}_{22}\text{O}_4\text{NSP}$
4	$p\text{-ClC}_6\text{H}_4$	80.6	88–89	2.98	2.90	$\text{C}_{24}\text{H}_{19}\text{O}_4\text{NSPCl}$
5	$o\text{-NO}_2\text{C}_6\text{H}_4$	86.2	112–113	5.65	5.66	$\text{C}_{24}\text{H}_{19}\text{O}_6\text{N}_2\text{SP}$
6	$\alpha\text{-C}_{10}\text{H}_7$	87.2	118–120	2.77	2.80	$\text{C}_{28}\text{H}_{22}\text{O}_4\text{NSP}$
7	$\beta\text{-C}_{10}\text{H}_7$	72.3	98–99	2.75	2.80	$\text{C}_{28}\text{H}_{22}\text{O}_4\text{NSP}$

TABLE 5

Monophenyl Esters of Arylsulfonamidophenylphosphinic Acids
 $\text{ArSO}_2\text{NHPO}(\text{C}_6\text{H}_5)(\text{OC}_6\text{H}_5)$

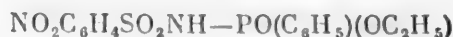
Prep. No.	Ar	Yield (%)	Melting point	Found equiv.*	Empirical formula
1	C_6H_5	89.1	144–146°	0.99	$\text{C}_{18}\text{H}_{16}\text{O}_4\text{NSP}$
2	$o\text{-CH}_3\text{C}_6\text{H}_4$	98.9	130–131	1.00	$\text{C}_{19}\text{H}_{18}\text{O}_4\text{NSP}$
3	$p\text{-CH}_3\text{C}_6\text{H}_4$	98.4	155–157	1.02	$\text{C}_{19}\text{H}_{18}\text{O}_4\text{NSP}$
4	$\alpha\text{-C}_{10}\text{H}_7$	85.6	165–166	1.03	$\text{C}_{22}\text{H}_{18}\text{O}_4\text{NSP}$
5	$p\text{-ClC}_6\text{H}_4$	99.1	124–125	0.99	$\text{C}_{18}\text{H}_{15}\text{O}_4\text{NSPCl}$
6	$p\text{-NO}_2\text{C}_6\text{H}_4$	98.2	120–121	0.99	$\text{C}_{18}\text{H}_{15}\text{O}_6\text{N}_2\text{SP}$

* Calculated equiv.: 1.00.



However, the arylsulfonamidophenylphosphinic acids or their monoalkyl esters cannot be isolated from the hydrolyzate.

Monoalkyl esters are very much more conveniently prepared directly from phenyldichlorophosphazosulfonaryls instead of by hydrolysis of dialkoxyposphazosulfonaryls: Addition of a benzene solution of phenyldichlorophosphazosulfonaryl to excess of sodium alkoxide solution leads to instantaneous formation of the sodium salt of the monoalkyl ester (Table 3). However, the monoethyl esters of *o*-, *m*-, and *p*-nitrophenylsulfonamidophenylphosphinic acids



cannot be obtained by this route: The reaction leads to black resins.

Monoalkyl esters of arylsulfonamidophenylphosphinic acids are colorless, crystalline substances, easily soluble in alcohol, less easily soluble in hot water, very sparingly soluble in benzene, ether, ligroine, CCl_4 , and other nonpolar solvents; they crystallize nicely from water or dilute alcohol. Chemically, the monoalkyl esters are monobasic acids titrating with sodium hydroxide solution to precisely one equivalent (in presence of phenolphthalein).

Aromatic esters of arylsulfonimidophenylphosphinic acids can be obtained by reaction of (I) with the appropriate sodium aryloxides. For example, reaction of phenyldichlorophosphazosulfonaryls with sodium phenoxide readily leads in good yield to formation of phenyldiphenoxyposphazosulfonaryls (diphenyl esters of arylsulfonimidophenylphosphinic acids) (IV) (Table 4).

Phenyldiphenoxyposphazosulfonaryls (IV) are colorless, crystalline substances, readily soluble in benzene, acetone, hot alcohol, and hot CCl_4 , insoluble in water, ether, and ligroine. They are perfectly resistant to water and do not react with it even on prolonged heating. In acid media they behave like phenyldialkoxyposphazosulfonaryls, and are hydrolyzed to aryl sulfamides. However, they differ from phenyldialkoxyposphazosulfonaryls and from triphenoxyposphazosulfonaryls, $\text{ArSO}_2\text{N}=\text{P}(\text{OC}_6\text{H}_5)_3$ (IV) [4], in being very much more sensitive to the action of caustic alkali; depending on the alkali concentration, the yield and character of the product of hydrolysis varies. Only by use of a very dilute aqueous alcoholic sodium hydroxide solution (0.02 N or lower) was it possible to perform smoothly the hydrolysis of (IV) in good yield with formation of monophenyl esters of arylsulfonamidophenylphosphinic acids (V) (Table 5).

Under the action of more highly concentrated sodium hydroxide solutions (0.1 N and higher), hydrolysis of phenyldiphenoxyposphazosulfonaryls leads to formation of resins from which the monophenyl esters cannot be isolated, although the latter are extremely resistant to the action of alkalis.

The monophenyl esters are colorless, crystalline substances, crystallizing nicely from dilute alcohol; insoluble in water, ether, and CCl_4 , highly soluble in acetone, benzene, and hot alcohol. Chemically, the monophenyl esters (V) are monobasic acids, titrating to exactly one equiv. with sodium hydroxide solution (in presence of phenolphthalein).

EXPERIMENTAL

Phenyldialkoxyposphazosulfonaryls (II) (dialkyl esters of arylsulfonamidophenylphosphinic acids) (Table 1). To a solution of 0.005 mole of phenyldichlorophosphazosulfonaryl (I) in 25 ml of benzene was added (with stirring and ice-water cooling), a solution of 0.01 g-atom of sodium (0.23 g) in 15 ml of alcohol at such a rate that the temperature did not rise above 10° . Into the reaction mixture was run 100-150 ml of water, the benzene layer was separated, and the aqueous layer again extracted with benzene. The benzene extracts were combined and dried with sodium sulfate, and the benzene was distilled off. Removal of the last traces of benzene (which hinder crystallization) was effected by holding in a vacuum for 2-3 hr. In the majority of cases, the esters "dried" in this way crystallized if merely rubbed with a glass rod. Solid esters were purified by crystallization from alcohol.

Hydrolysis of (II) (Table 2). To 0.002 mole of phenyldialkoxyposphazosulfonyl was added 25 ml of 0.4 N aqueous alcoholic sodium hydroxide (5 ml of 2 N aqueous NaOH + 20 ml of alcohol). The mixture was heated for 3 hr on a water bath, after which the excess of alcohol was distilled off in vacuo. Acidification of the residue with HCl to an acidic reaction led to precipitation of sparingly soluble monoalkyl esters (III); these were collected and washed with water. Purification was effected by recrystallization from 50% alcohol.

Monoalkyl esters of arylsulfonamidophenylphosphinic acids (III) (directly from phenyldichlorophosphazosulfonyls) (Table 3). Anhydrous alcohol (10 ml) and sodium (0.01 g-atom) were placed in a three-necked flask fitted with reflux condenser, stirrer, and dropping funnel. After the sodium had dissolved, a solution of 0.003 mole of phenyldichlorophosphazosulfonyl (I) in 10 ml of benzene was introduced dropwise with vigorous stirring. The mixture was heated for 0.5 hr at 50°, after which the benzene and alcohol were distilled off in vacuo on a water bath. The dry residue was dissolved in 10 ml of water and acidified with HCl until acid to Congo. The crystalline precipitate was collected and washed well with water. Purification was effected by recrystallization from 50% alcohol.

Phenyldiphenoxyposphazosulfonyls (IV) (Table 4). A solution of 0.005 mole of phenyldichlorophosphazosulfonyl (I) in 25 ml of benzene was run into 0.01 mole of dry sodium phenoxide, after which the mixture was heated for an hour on a water bath. After the NaCl had been separated, the benzene was distilled off from the filtrate, and the oily residue was kept in vacuo for 2-3 hr for removal of traces of benzene. Diphenyl esters (IV) "dried" in this way crystallize with facility. They were purified by crystallization from alcohol.

Hydrolysis of (IV) (Table 5). To 0.003-0.004 mole of phenyldichlorophosphazosulfonyl (IV) was added 250 ml of 0.02 N aqueous alcoholic sodium hydroxide (50 ml of 0.1 N aqueous NaOH + 200 ml of alcohol), and the mixture heated for 3 hr on a water bath. The excess alcohol was then taken off in vacuo and the aqueous residue acidified until it had an acid reaction. The precipitated monophenyl esters (V) were separated, washed with water, and crystallized from dilute alcohol.

SUMMARY

1. The dimethyl, diethyl, and diphenyl esters of arylsulfonamidophenylphosphinic acids were synthesized. Their hydrolysis was effected.
2. A series of monoalkyl and monophenyl esters of arylsulfonamidophenylphosphinic acids was prepared.

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DIPHENYLCHLOROPHOSPHAZOSULFONARYLS

V. I. Shevchenko, V. T. Stratienko, and A. M. Pinchuk

Dnepropetrovsk Metallurgical Institute

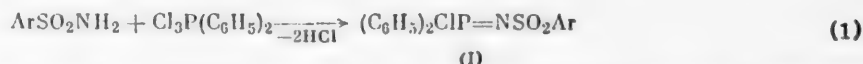
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Phenyldichloro- and diphenylchlorophosphazosulfonaryls are intermediate links in a series of compounds obtained by successive replacement of chlorine atoms in trichlorophosphazosulfonaryls by phenyl radicals: $\text{ArSO}_2\text{N} = \text{PCl}_3$, $\text{ArSO}_2\text{N} = \text{P}(\text{C}_6\text{H}_5)\text{Cl}_2$, $\text{ArSO}_2\text{N} = \text{P}(\text{C}_6\text{H}_5)_2\text{Cl}$, $\text{ArSO}_2\text{N} = \text{P}(\text{C}_6\text{H}_5)_3$. Since trichloro- and phenyldichlorophosphazosulfonaryls are easily obtained in good yield by the Kirsanov phosphazo reaction - interaction of acylamides with phosphorus pentahalides [1] or their derivatives [2] - it was expected that diphenylchlorophosphazosulfonaryls could also be prepared by this reaction. This expectation was fully confirmed experimentally.

Interaction of arylsulfamides with diphenylphosphorus trichloride led in good yield to diphenylchlorophosphazosulfonaryls (I) by Eq. (1) (Table 1).



Reaction of arylsulfamides with diphenylphosphorus trichloride takes place in the course of 1.5-2 hr at 125-135°, whereas the reaction with phenylphosphorus tetrachloride proceeds smoothly at 75-100° and is completed in 20 to 30 min, and phosphorus pentachloride reacts with even greater facility; trichlorophosphazosulfonaryls are easily prepared in carbon tetrachloride solution, even at the boiling point of the solvent. Heating of equimolar quantities of arylsulfamides with diphenylphosphorus trichloride for 1.5-2 hr enables 90-95% of the hydrogen chloride to be trapped. At the same time, resinous products are usually obtained and can be readily brought into the crystalline state by treatment with carbon tetrachloride, ether, or other suitable solvent. This treatment probably brings the secondary reaction products into solution, and the sparingly soluble phosphazo compounds come down in the crystalline state in a sufficiently high degree of purity. The products of hydrolysis of the resulting diphenylchlorophosphazosulfonaryls exactly titrate to two equivalents.

Diphenylchlorophosphazosulfonaryls can also be prepared by interaction of diphenylchloroarsine with sodium salts of chloramides of aromatic sulfonic acids [Eq. (2)].



However, this reaction is less convenient since it is accompanied by formation of a large amount of secondary products. One treatment of the reaction mixture with carbon tetrachloride or other suitable solvent is inadequate, and the preparation of a relatively pure product calls for several crystallizations. This is extremely undesirable, in view of the ease of hydrolysis of halogen-containing phosphazo compounds. Diphenylchlorophosphazosulfonphenyl obtained by reaction (2) was found to be identical with the product of reaction (1).

Diphenylchlorophosphazosulfonaryls are colorless crystalline substances, easily hydrolyzed by moisture of the air (for example, the products of hydrolysis titrated to 1.5-1.7 equivalents after standing for 6 months in loosely closed containers in a desiccator over sulfuric acid). Readily soluble in hot benzene and ethyl acetate, sparingly soluble in ether and carbon tetrachloride, insoluble in ligroine and water. They crystallize readily from ethyl acetate or benzene in the form of fine prisms or thin, short needles. In chemical properties (I) are acid chlorides, readily reacting with alcohols, amines, and phenoxides.

Diphenylchlorophosphazosulfonaryls are easily hydrolyzed by water with formation of arylsulfonamidodiphenylphosphinic acids (II) according to Eq. (3) (Table 2).

TABLE 1

Diphenylchlorophosphazosulfonyls $(C_6H_5)_2ClP = NSO_2Ar$

Ar	Yield (%)	Melting point	Found equiv.* (after hydrolysis)	Empirical formula
C_6H_5	90.5	109–111°	2.01	$C_{18}H_{15}O_2NSPCl$
<i>o</i> - $CH_3C_6H_4$	93.0	129–130	1.96	$C_{19}H_{17}O_2NSPCl$
<i>p</i> - $CH_3C_6H_4$	88.0	99–101	1.95	$C_{19}H_{17}O_2NSPCl$
<i>α</i> - $C_{10}H_7$	51.0	114–116	1.96	$C_{22}H_{17}O_2NSPCl$
<i>β</i> - $C_{10}H_7$	90.5	135–138	2.12	$C_{22}H_{17}O_2NSPCl$
<i>o</i> - $NO_2C_6H_4$	99.8	159–161	2.02	$C_{18}H_{14}O_4N_2SPCl$
<i>m</i> - $NO_2C_6H_4$	87.0	118–120	1.99	$C_{18}H_{14}O_4N_2SPCl$
<i>p</i> - $NO_2C_6H_4$	72.7	164–168	1.99	$C_{18}H_{14}O_4N_2SPCl$
<i>p</i> - ClC_6H_4	101.3	Forms tar	2.02	$C_{18}H_{14}O_4N_2SPCl_2$

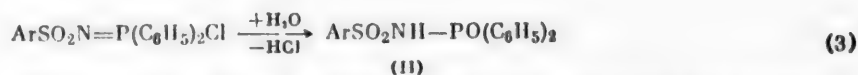
*Calculated equiv.: 1.00.

TABLE 2

Arylsulfonamidodiphenylphosphinic Acids $ArSO_2NH - PO(C_6H_5)_2$

Ar	Yield (%)	Melting point	Equiv. found*	Empirical formula
C_6H_5	98.0	205–206°	0.99	$C_{18}H_{16}O_3NSP$
<i>o</i> - $CH_3C_6H_4$	96.2	183–184	0.98	$C_{19}H_{18}O_3NSP$
<i>p</i> - $CH_3C_6H_4$	81.5	214–215	0.98	$C_{19}H_{18}O_3NSP$
<i>α</i> - $C_{10}H_7$	97.5	212–213	0.99	$C_{22}H_{18}O_3NSP$
<i>β</i> - $C_{10}H_7$	98.5	213.5–214	1.02	$C_{22}H_{18}O_3NSP$
<i>o</i> - $NO_2C_6H_4$	93.5	199–200	1.028	$C_{18}H_{15}O_5N_2SP$
<i>m</i> - $NO_2C_6H_4$	98.7	192–193	1.00	$C_{18}H_{15}O_5N_2SP$
<i>p</i> - $NO_2C_6H_4$	98.3	204–205	1.01	$C_{18}H_{15}O_5N_2SP$
<i>p</i> - ClC_6H_4	96.2	220–221	0.99	$C_{18}H_{15}O_5N_2SPCl$

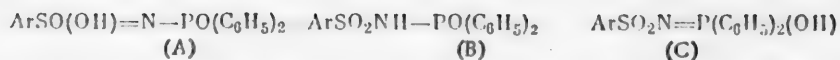
*Calculated equiv.: 1.00.



Benzene-insoluble acids (II) start to come down after only 15 min if benzene solutions of the phosphazo compounds are stood in a desiccator containing water. However, the crystalline diphenylchlorophosphazosulfonyls are hydrolyzed very slowly in water or aqueous sodium hydroxide, since neither the phosphazo compounds themselves nor the products of their hydrolysis — arylsulfonamidodiphenylphosphinic acids (II) — are soluble in water. Diphenylchlorophosphazosulfonyls dissolve relatively quickly in boiling aqueous sodium hydroxide, with formation of sodium salts of the acids, while the free acids (II) come down when the alkaline hydrolyzate is acidified.

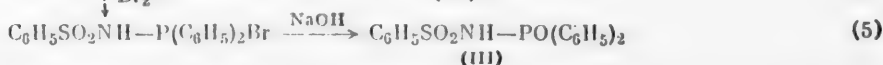
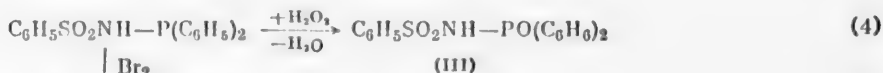
Arylsulfonamidodiphenylphosphinic acids are colorless, crystalline substances, with relatively high solubility in hot alcohol; very sparingly soluble in benzene; insoluble in water, ether, and carbon tetrachloride. They readily crystallize from alcohol in the form of well-developed fine prisms or slender, small needles. With an aqueous sodium hydroxide solution the acids titrate to one equivalent (with phenolphthalein). They are extremely resistant to hydrolysis (*β*-naphthylsulfonamidodiphenylphosphinic acid is recovered unchanged after heating for one hour in 0.1 N aqueous alcoholic hydrochloric acid).

Three tautomeric forms are possible for arylsulfonamidodiphenylphosphinic acids.



Diphenylchlorophosphazosulfonyls can therefore be regarded as acid chlorides of acids existing in the imido form (C), i.e., as acid chlorides of arylsulfonimidodiphenylphosphinic acids. It may be conjectured that the amide form (B) will be the most stable of the three tautomeric forms, since the N-H bond is less polarized than the O-H bond.

Arylsulfonamidodiphenylphosphinic acids can also be obtained by oxidation with hydrogen peroxide, or by bromination followed by hydrolysis of N-diphenylphosphinaryl sulfamides [Eqs. (4) and (5)]. As an example, N-diphenylphosphinbenzenesulfamide, easily prepared from diphenylchlorophosphine and the sodium salt of benzenesulfamide, is oxidized by hydrogen peroxide with formation of phenylsulfonamidodiphenylphosphinic acid (III) in over 70% yield.



Phenylsulfonamidodiphenylphosphinic acid [obtained by reactions (4) and (5)], was found to be identical with the phenylsulfonamidodiphenylphosphinic acid prepared by reaction (3).

N-Diphenylphosphinbenzenesulfamide is a viscous, oily liquid, easily hydrolyzed by atmospheric moisture at the N-P bond with formation of benzenesulfamide. Since N-diphenylphosphinbenzenesulfamide does not distill without decomposition (3-4 mm, vacuum), it was used in further reactions in this work without isolation in the pure state.

EXPERIMENTAL

Diphenylchlorophosphazosulfonyls (I). A mixture of 0.02 mole of arylsulfamide and 0.02 mole of diphenylphosphorus trichloride was heated on an oil bath until melted (100-105°). Hydrogen chloride started to come off briskly at 115-120°. After frothing of the reaction mixture had ceased, the bath temperature was raised to 125-130° and held for 1.5-2 hr. The reaction had been substantially completed after this period, and over 90% of the hydrogen chloride had been evolved. Heating of the mixture to 150° resulted in completion of the reaction after 30 min.

The reaction mixture must be heated to 170-175° for the preparation of diphenylchlorophosphazosulfon-o- and -p-nitrophenyls, since the resulting phosphazo compounds readily crystallize, and the initially liquefying reaction mixture again sets to a crystalline mass even at 150°, so that the reaction slows down or is entirely suppressed. By the procedure described, diphenylchlorophosphazosulfon-p-nitrophenyl is obtained at once in the form of a crystalline mass, especially if the reaction mixture is kept for some time, after completion of reaction, at 110-120°, at which temperature crystallization goes relatively quickly.

The remaining phosphazo compounds are obtained in the form of resins, which can, however, be converted with facility into crystalline products by treatment with a suitable solvent. The latter is added to the resinous product and the mixture stirred with heating. The phosphazo compounds come down in crystal form and are suction-filtered and washed thoroughly. The diphenylchlorophosphazosulfonyls obtained in this manner are fairly pure and suitable for use without recrystallization. Diphenylchlorophosphazosulfonphenyl readily passes into the crystalline state if worked up only with absolute ether; ethyl acetate is a more convenient solvent in the case of diphenylchlorophosphazosulfon-β-naphthol, as well as of o- and m-nitrophenyls; the latter can be at once recrystallized from this solvent; the remaining phosphazo compounds are worked up with carbon tetrachloride.

Diphenylchlorophosphazosulfon-p-chlorophenyl could not be obtained at all in the crystalline state: The reaction mixture formed a viscous, oily liquid which did not crystallize on cooling. It dissolved readily in ether and benzene, but treatment of the solution with ligroine led to separation of the noncrystallizing, oily liquid.

The crystalline diphenylchlorophosphazosulfonyls can be recrystallized from benzene, ethyl acetate, or other solvent, but this is unnecessary since both the unrecrystallized and the recrystallized products titrate exactly to two equivalents.

Arylsulfonamidodiphenylphosphinic acids (II) (by hydrolysis of diphenylchlorophosphazosulfonyls). To 0.05 mole of (I) was added 125-130 ml of 0.1 N aqueous sodium hydroxide. Heat was applied until solution took place. Acidification of the alkaline neutralizate led to precipitation of water-insoluble products (II) which were suction-filtered and washed well with water. The arylsulfonamidodiphenylphosphinic acids crystallized from alcohol in the form of slender needles or fine prisms.

Phenylsulfonamidodiphenylphosphinic acid (III) (by oxidation of N-diphenylphosphinbenzenesulfamide). a) To a solution of 0.02 mole of diphenylchlorophosphine in 50 ml of dry benzene was added 0.02 mole of the sodium salt of benzenesulfamide. The mixture was refluxed for 20-30 min on a water bath. To the resulting benzene solution of N-diphenylphosphinbenzenesulfamide was added (without separation of the sodium chloride) 30 ml of ligroine, and the mass was thoroughly shaken. The precipitated acid was suction-filtered and washed with water and alcohol. Yield 65-70%. Long prisms, m.p. 205-207° (from alcohol). A mixture with the acid obtained by hydrolysis of diphenylchlorophosphazosulfonylphenyl did not give a depression of melting point.

Equiv. found: 1.00. Calculated equiv.: 1.00.

b) To a solution of 0.02 mole of N-diphenylphosphinbenzenesulfamide, prepared in similar fashion, was added (good stirring), 0.023-0.025 mole of bromine dissolved in 10 ml of benzene. N-Diphenyldibromophosphinylbenzenesulfamide came down in the form of a red, oily layer, and was separated from solvent and treated with 0.1 N sodium hydroxide solution in excess. The alkaline hydrolyzate was acidified until it had an acid reaction, and the semicrystalline precipitate was repeatedly reprecipitated; in these reprecipitations, less alkali was taken in each successive operation than was needed for complete solution of the precipitate. M.p. 205-207° (from alcohol). A mixture with the acid obtained by hydrolysis of diphenylchlorophosphazosulfonylphenyl or by oxidation of diphenylphosphinbenzenesulfamide with hydrogen peroxide melted without depression of melting point. Yield 15-20%.

Equiv. found: 1.01. Equiv. calculated: 1.00.

SUMMARY

1. Reaction of arylsulfamides with diphenylphosphorus trichloride gave diphenylchlorophosphazosulfonyls.
2. Hydrolysis of diphenylchlorophosphazosulfonyls gave arylsulfonamidodiphenylphosphinic acids.
3. An alternative synthesis of phenylsulfonamidodiphenylphosphinic acid involved oxidation of diphenylphosphinbenzenesulfamide with hydrogen peroxide.

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*Original Russian pagination. See C.B. translation.

SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

XIV. OXIDATIVE CHLOROPHOSPHINATION OF VINYL CHLORIDE BY METHYLDICHLOROPHOSPHINE AND THE PREPARATION OF SOME ESTERS OF DIALKYLPHOSPHINIC ACIDS

Yu. M. Zinov'ev and L. Z. Soborovskii

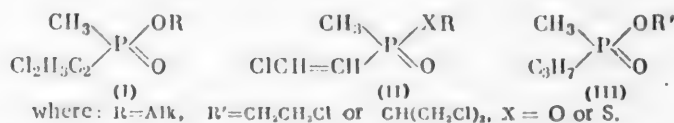
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Full esters of halogenated alkanephosphinic acids have been described in the literature [1]. But esters of secondary phosphinic acids containing halogen in an alkyl radical at the phosphorus have not previously been known.

In the present work, we obtained chlorine-containing alkyl esters of dialkylphosphinic acids with the structure:



Starting substances for preparation of esters of this type were the acid chlorides of methyldichloroethylphosphinic (I), methyl-2-chloroethenylphosphinic (II), and methylpropylphosphinic (III) acids. The first two acid chlorides were prepared for the first time by oxidative chlorophosphination of vinyl chloride by methyldichlorophosphine; the third has already been described [2].

The formation of two acid chlorides (I and II) by oxidative chlorophosphination of vinyl chloride by methyldichlorophosphine is probably associated with partial dehydrochlorination of (I) during distillation. A similar process was observed during distillation of the diacid chloride of cyclohexanephosphinic acid [3].

Oxidative chlorophosphination of vinyl chloride by phosphorus trichloride yields isomeric acid chlorides of dichloroethanephosphinic acid [1]. In all probability, the same process takes place during oxidative chlorophosphination of vinyl chloride by phosphorus trichloride derivatives of the type of RPCl_2 , and in particular by methyldichlorophosphine. Esters obtained from the various alcohols and the acid chloride resulting from reaction between methyldichlorophosphine, vinyl chloride, and oxygen are therefore probably mixtures of isomeric compounds.

In the present work, we did not undertake the isolation of pure substances from the possible mixture of isomers. Full structural formulas of the compounds prepared are therefore not given in the table.

EXPERIMENTAL

1. Acid chlorides of methyldichloroethylphosphinic (I) and methylchloroethenylphosphinic (II) acids. a) Oxygen was passed at -20° through a mixture of 170 g (2.72 moles) of vinyl chloride and 120 g (1.03 moles) of methyldichlorophosphine (with b.p. $79-80^\circ$)^{*} until the reaction came to an end. There was isolated 20.5 g of liquid boiling over the range of 65 to 120° (4 mm). Two fractions were obtained on fractional distillation: 105 to 107° (4 mm), and $70-75^\circ$ (4 mm).

^{*} According to the literature, it has b.p. $77-79^\circ$ [4].

Compound	Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	M_n		Yield (%)
					found	calc.	
(I)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{Cl}$	105—107° (4)	1.4820	1.4960	38.45	38.60	61.0
(II)	$\text{CH}_3(\text{ClCH}=\text{CH})\text{P}(\text{O})\text{Cl}$	70—75 (4)	1.3657	1.4950	33.94	33.27	—
(III)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{OCH}_3$	95—100 (4)	1.3432	1.4668	39.40	39.63	21.8
(IV)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{OC}_2\text{H}_5$	88—92 (2)	1.2972	1.4560	42.36	44.25	61.3
(V)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{OC}_3\text{H}_7$	94—96 (2)	1.2412	1.4530	47.85	48.86	47.5
(VI)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{OCH}(\text{CH}_3)_2$	110—112 (5)	1.2423	1.4530	47.63	48.86	22.4
(VII)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{O}(\text{CH}_2)_3\text{CH}_3$	122—126 (3)	1.2087	1.4570	52.2	53.48	33.5
(VIII)	$\text{CH}_3(\text{C}_2\text{H}_5\text{Cl}_2)\text{P}(\text{O})\text{OCH}_2\text{CH}(\text{CH}_3)_2$	115—120 (3)	1.2096	1.4560	52.37	53.48	27.4
(IX)	$\text{CH}_3(\text{ClCH}=\text{CH})\text{P}(\text{O})\text{OC}_2\text{H}_5$	55—58 (2.5)	1.1533	1.4520	39.45	38.91	74.5
(X)	$\text{CH}_3(\text{ClCH}=\text{CH})\text{P}(\text{O})\text{SC}_2\text{H}_5$	80—85 (2)	1.2360	1.5250	45.77	45.34	19.7
(XI)	$\text{CH}_3(\text{C}_3\text{H}_7)\text{P}(\text{O})\text{OC}_2\text{H}_4\text{Cl}$	113—114 (4)	1.1574	1.4595	43.55	44.00	57.0
(XII)	$\text{CH}_3(\text{C}_3\text{H}_7)\text{P}(\text{O})\text{OCH}(\text{CH}_2\text{Cl})_2$	135—139 (2)	1.2114	1.4715	53.78	53.48	66.0

Higher boiling fraction (I):

Found % C 18.06, 18.34; H 2.91, 2.33. $\text{C}_3\text{H}_5\text{OPCl}_2$. Calculated % C 18.43; H 3.09.

Lower boiling fraction (II):

Found % C 22.98, 22.72; H 3.36, 3.15. $\text{C}_3\text{H}_5\text{OPCl}_2$. Calculated % C 22.66; H 3.17.

b) From 100 g (1.6 moles) of vinyl chloride and 25 g (0.214 mole) of methyldichlorophosphine, under the conditions of a, was obtained 12.7 g of (I).

2. Methyl ester of methyldichloroethylphosphinic acid (III). At -5° , 70 g (0.036 mole) of (I) was run into 45 ml of methanol to give 1.5 g of (III).

Found % C 26.04, 26.24; H 4.98, 5.10; OCH_3 16.67, 16.22. $\text{C}_4\text{H}_9\text{O}_2\text{PCl}_2$. Calculated % C 25.15; H 4.75; OCH_3 16.24.

3. Ethyl ester of methyldichloroethylphosphinic acid (IV). Preparation under the conditions of experiment 2 from 7.0 g of (I) and 50 ml of alcohol, gave 4.5 g of (IV).

Found % C 28.38, 28.15; H 4.20, 4.98, P 14.57; OC_2H_5 21.05. $\text{C}_6\text{H}_{11}\text{O}_2\text{PCl}_2$. Calculated % C 29.29; H 5.40; P 15.11; OC_2H_5 21.98.

4. Propyl ester of methyldichloroethylphosphinic acid (V). From 7.0 g of (I) and 40 ml of propanol was obtained 3.71 g of (V).

Found % C 32.80, 32.97; H 6.24, 6.12; P 13.66, 13.85; OC_3H_7 26.71, 27.01. $\text{C}_6\text{H}_{13}\text{O}_2\text{PCl}_2$. Calculated % C 32.89; H 5.98; P 14.14; OC_3H_7 26.07.

5. Isopropyl ester of methyldichloroethylphosphinic acid (VI). From 8 g of (I) and 40 ml of isopropyl alcohol was obtained 2 g of (VI).

Found % C 33.75, 33.73; H 5.70, 5.87; OC_3H_7 26.53, 26.56. $\text{C}_6\text{H}_{13}\text{O}_2\text{PCl}_2$. Calculated % C 32.89; H 5.98; OC_3H_7 26.97.

6. Butyl ester of methyldichloroethylphosphinic acid (VII). From 5.3 g of (I) and 30 ml of butanol was obtained 2.1 g of (VII).

Found % C 35.12, 35.39; H 6.59, 6.78; P 12.64. $\text{C}_7\text{H}_{15}\text{O}_2\text{PCl}_2$. Calculated % C 36.07; H 6.48; P 13.29.

7. Isobutyl ester of methyldichloroethylphosphinic acid (VIII). From 7 g of (I) and 45 ml of isobutanol was obtained 2.3 g of (VIII).

Found % C 36.61, 36.36; H 6.70, 6.43. $\text{C}_7\text{H}_{15}\text{O}_2\text{PCl}_2$. Calculated % C 36.07; H 6.48.

8. Ethyl ester of methyl-2-chloroethenylphosphinic acid (IX). From 10 g (0.063 mole) of (II) and 50 ml of ethanol, under the conditions of experiment 2, was obtained 7.9 g of (IX).

Found %: C 35.39, 35.67; H 6.64, 6.85. $C_5H_{10}O_2PCl$. Calculated %: C 35.62; H 5.98.

9. Ethyl ester of methyl-2-chloroethenylthiophosphinic acid (X). To a solution of 5.3 g (0.033 mole) of (II) in 50 ml of ether was added, at 0°, 2.84 g of sodium ethylmercaptide. After 3 hr, the precipitated NaCl was filtered off and 1.2 g of (X) was isolated.

Found %: C 31.74, 31.28; H 5.30, 5.03; S 16.48, 16.03. $C_5H_{10}OPSCl$. Calculated %: C 32.52; H 5.45; S 17.36.

10. 2-Chloroethyl ester of methylpropylphosphinic acid (XI). A solution of 8 g (0.57 mole) of methylpropylphosphinyl chloride [2] in 20 ml of ether was mixed at 0° with a solution of 5 g (0.062 mole) of 2-chloroethanol in ether. There was isolated 6.0 g of (XI).

Found %: C 39.25, 39.18; H 8.15, 7.72; P 17.18; 17.20. $C_6H_{14}O_2PCl$. Calculated %: C 39.03; H 7.62; P 16.78.

11. 1,3-Dichloroisopropyl ester of methylpropylphosphinic acid (XII). Reaction of 8 g of methylpropylphosphinyl chloride and 7.7 g (0.06 mole) of 1,3-dichloroisopropyl alcohol under the conditions of experiment 10 gave 8.8 g of (XII).

Found %: C 36.79, 36.77; H 6.80, 6.92; P 13.64, 13.66. $C_7H_{15}O_2PCl_2$. Calculated %: C 36.07; H 6.48; P 13.29.

SUMMARY

1. Oxidative chlorophosphination of vinyl chloride was effected with methyldichlorophosphine; methyldichloroethylphosphinyl and methyl-2-chloroethenylphosphinyl chlorides were prepared.

2. The following were synthesized: the methyl, ethyl, propyl, isopropyl, butyl, and isobutyl esters of methyldichloroethylphosphinic acid, the ethyl ester of methyl-2-chloroethenylthiophosphinic acid, and the 2-chloroethyl and 1,3-dichloroisopropyl esters of methylpropylphosphinic acid.

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ORGANIC COMPOUNDS OF SULFUR

V. SYNTHESIS AND SOME PROPERTIES OF HALOACETYLENESULFOCHLORIDES

B. M. Gladshtein and L. Z. Soborovskii

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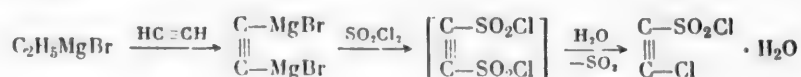
Original article submitted May 27, 1959

Numerous attempts have been made to prepare compounds containing a sulfo group [1] at an acetylenic carbon atom.

Rondestvedt and Wygant [2] described some unsuccessful attempts to synthesize acetylenesulfonyl chloride by sulfonation of phenylacetylene and its sodium derivative with the help of dioxane sulfotrioxide and sulfur dioxide, as well as by dehydrobromination of α -bromoethenesulfochloride and sodium α -bromostyrenesulfonate. For example, treatment of α -bromoethenesulfochloride with triethylamine in ethereal solution at 70° resulted in precipitation of triethylamine hydrobromide, and a substance was isolated with a boiling point close to that of vinyl sulfochloride. The analytical data were unsatisfactory. The infrared spectrum of the substance did not contain frequencies in the 4.4-4.6 μ region (the C \equiv CH bond) and differed from the infrared spectra of vinyl sulfochloride and of the original α -bromovinyl sulfochloride. In view of this, the authors consider the substance in question to be impure acetylenesulfochloride. Experiments on dehydrobromination of α -bromostyrenesulfochloride and sodium α -bromostyrenesulfonate, with the help of alcoholic alkali, triethylamine, and 2,6-lutidine, likewise did not lead to the desired derivative of acetylenesulfonic acid.

Dombrovskii and Prilutskii [3] succeeded in preparing the barium and potassium salts of 1-hexyne-1-sulfonic acid from 1-hexyne, and the barium and potassium salts of phenylacetylenesulfonic acid from phenylacetylene. However, the free acetylenesulfonic acid could not be isolated, since the substance decomposes completely during evaporation of its aqueous solution. Backer and Strating [4] isolated a substance containing the sulfo group at the acetylenic carbon when they synthesized bis-(tert-butylsulfonyl)-acetylene.

In the present work, the following route to a sulfochloride of the acetylenic series was selected, and the synthesis was accomplished:



A substance was obtained (yield about 10%, calculated on the ethyl bromide taken) which decolorized potassium permanganate solution, released iodine from potassium iodide solution, gave (after some time) a characteristic precipitate with Ilosvay reagent, and reacted violently (with detonation) with aniline. The structure of β -chloroacetylenesulfochloride hydrate was assigned to the product. Its crystalline aniline derivative corresponded in composition to β -phenylaminoacetylenesulfonic acid anilide dihydrochloride [$\text{C}_6\text{H}_5\text{NH}-\text{C}\equiv\text{C}-\text{SO}_2\text{NHC}_6\text{H}_5$] \cdot 2HCl.

Closer investigation of β -chloroacetylenesulfochloride hydrate revealed certain properties relating it to analogous compounds of the ethane and ethylene series, but also specific properties characterizing it unequivocally as an acetylenic derivative. For example, β -chloroacetylenesulfochloride hydrate is even more easily desulfonated under the action of aqueous bases than halogen-substituted sulfonic acids of the ethane and ethylene series [5]. Even aqueous ammonia (1:1) decomposes β -chloroacetylenesulfochloride with formation of SO_3^{--} ions in solution.

The action of Ilosvay reagent on β -chloroacetylenesulfochloride can be expressed by the equation:



Formation of a precipitate of copper chloroacetylide with Ilosvay reagent is characteristic of an α -acetylenic compound, and is evidently the result of preliminary transformation of the original sulfochloride by aqueous ammonia into chloroacetylene and subsequent precipitation of the latter by ions of monovalent copper.

The characteristic properties of β -chloroacetylenesulfochloride include the reaction with bromine in carbon tetrachloride, which is accompanied by decolorization of the bromine solution. Under the same conditions, β -chloroethenesulfochloride does not decolorize a solution of bromine in carbon tetrachloride.

It is interesting to note that the 1760 cm^{-1} frequency is present in the infrared spectrum of β -chloroethenesulfochloride hydrate and no frequencies are found in the 1960 cm^{-1} region (the characteristic frequency of acetylenic compounds).*

In this connection, we must remember that, on the basis of the infrared spectrum of bis-(ethoxycarbamino)-acetylene (I), Gaylord [6] assigned to this compound the structure of the isomeric bis-(carbethoxy)-glyoxaldimine (II).



It is possible that the unusual structure of β -chloroacetylenesulfochloride (a heavy concentration of substituents at triply bonded carbon atoms) lowers the characteristic frequency of this compound, just as replacement of hydrogen atoms in acetylene by deuterium lowers the characteristic frequencies in the acetylene spectrum from 1974 to 1750 cm^{-1} in the deuterioacetylene spectrum [7].

The foregoing data permit the conclusion that the structure of β -chloroacetylenesulfochloride hydrate can be assigned to the prepared substance in the light of its empirical formula, the chemical properties (behavior toward potassium permanganate solution, bromine in carbon tetrachloride, aqueous ammonia, and Ilosvay reagent) and the analysis of its aniline derivative. The structure in question also follows from the method of synthesis. Ordinary means for binding water (treatment with anhydrous salts and azeotropic distillation) did not lead to isolation of β -chloroacetylenesulfochloride in the anhydrous form.

In the present work, we investigated the behavior of β -chloroacetylenesulfochloride hydrate toward various fluorinating agents with the objective of preparing the corresponding sulfofluorides of the acetylenic series. β -Chloroacetylenesulfochloride reacts vigorously with pulverized potassium fluoride with formation of a fluorine-containing substance whose constants differed from those of the starting substance. We were unable, however, to separate β -chloroacetylenesulfofluoride in the analytically pure form. Analysis of the substance resulting from the action of potassium fluoride indicates that it is an approximately 45:55 mixture of the original β -chloroacetylenesulfochloride and chloroacetylenesulfofluoride. An aqueous solution of potassium fluoride completely decomposes β -chloroacetylenesulfochloride. Treatment of β -chloroacetylenesulfofluoride hydrate with zinc chloride in a platinum test tube at 150° does not give fluorine-containing substances. We have reported earlier [8] on other attempts to prepare sulfofluorides of the acetylenic series.

EXPERIMENTAL

β -Chloroacetylenesulfochloride (I).* A stream of purified acetylene was passed for 16 hr into ethylmagnesium bromide prepared from 1 mole of ethyl bromide. An Iotsich complex was prepared in a special two-necked flask fitted with a tap through which the complex was then added dropwise, with ice-salt cooling, to an ethereal solution of 135 g of freshly distilled sulfuryl chloride. After completion of this operation, the mixture was stirred for another hour at room temperature, and then poured onto ice. The ethereal layer was twice washed with iced water, dried with calcined sodium sulfate, and fractionally distilled.

B.p. $90-92^\circ$ (10 mm), n_D^{20} 1.5330, d_4^{20} 1.8781.

Found %: C 12.91, 12.59; H 1.18, 1.11; Cl 40.14, 40.07. $\text{C}_2\text{H}_2\text{O}_3\text{SCl}_2$. Calculated %: C 13.56; H 1.13; Cl 40.06.

*Spectral investigations by N. P. Rodionova and E. M. Popov.

**With participation of V. N. Chernetskii.

β -Phenylaminoacetylenesulfonic acid anilide dihydrochloride (II). Freshly distilled aniline was added, dropwise with shaking and cooling, to 2 g of (I) in 8 ml of ether. The mixture was treated with 10% hydrochloric acid solution and washed with water; the precipitate was twice recrystallized from ethanol. Pale-yellow crystals with m.p. 130-131°.

Found %: C 48.99, 49.40; H 4.03, 4.25; S 9.24, 9.48; N 8.53, 8.52. $C_{14}H_{14}O_2N_2SCl_2$. Calculated %: C 48.70; H 4.08; S 9.28; N 8.11.

Action of aqueous ammonia on (I). 0.5 g of (I) was treated with 3 ml of water, and 2 ml of ammonia solution (1:1) was added; after 5 min, barium chloride solution was added. A white crystalline precipitate came down; soluble in nitric acid (1:1).

Action of Ilosvay reagent on (I). To a solution of 1 g of (I) in 10 ml of acetone was added 20 ml of water, followed (with stirring) by 50 ml of freshly prepared Ilosvay reagent (containing 0.46 g of Cu^+). Considerable heat was generated and a red precipitate formed. The reaction mass was treated with 50 ml of water and stood overnight. The precipitate was washed three times on the filter with water, twice with acetone, then with ether, and dried. No copper ions were detected in the filtrate. A solution of a sample of the precipitate in concentrated nitric acid gave positive reactions for chlorine and copper; another sample was fused with sodium and gave a negative test for sulfur; a third sample gave a positive color reaction [9] for carbon.

Action of bromine on (I). A solution of bromine in carbon tetrachloride was added to a solution of (I) in the same solvent; the bromine solution decolorized. Under the same conditions, β -chlorovinylsulfochloride does not decolorize bromine solution.

Action of zinc fluoride on (I). In a platinum test tube, 6.8 g of (I) was heated with 7.5 g of zinc fluoride at 150° for 6 hr. The resulting liquid had b.p. 55.5-57° (4 mm), n_D^{20} 1.5560, d_4^{20} 2.1896, did not contain fluorine, and contained 8.69% of chlorine. It was not further examined.

Action of potassium fluoride on (I). To 24.8 g of (I) was added portionwise 33 g (100% excess) of finely pulverized, freshly calcined potassium fluoride. During this operation the temperature rose spontaneously to 50 to 60°. The mixture was heated in vacuo (bath temperature 80°), while the residual pressure was held at first at 85 mm, and later at 15 mm, and subjected to fractional distillation. A colorless, mobile, lachrymatory liquid, soluble in organic solvents (ether, acetone, chloroform); insoluble in water.

b.p. 51-55° (15 mm), n_D^{20} 1.4985, d_4^{20} 2.0501.

Found %: C 16.72, 17.06; F 7.57, 6.84; Cl 31.64, 31.62. M 291.5. $C_2O_2SCl_2 + C_2O_2SFCI$. Calculated %: C 16.04; F 7.57; Cl 31.43.

In its composition, the substance corresponds to a mixture of β -chloroacetylenesulfofluoride and β -chloroacetylenesulfochloride in the ratio of 55.3:44.7. It is probably an azeotropic mixture.

Action of chlorine on (I). A solution of 2.5 g of (I) in 15 ml of carbon tetrachloride was chlorinated with exposure to light. Slight heating was observed during chlorination. A substance was obtained with b.p. 75-79° (10 mm), n_D^{20} 1.5148. It was not investigated more closely.

SUMMARY

1. β -Chloroacetylenesulfochloride was synthesized in the form of the hydrate, and some of its properties were studied: behavior toward aqueous ammonia, bromine, chlorine, potassium fluoride, zinc fluoride, Ilosvay reagent, and aniline.

2. β -Phenylaminoacetylenesulfonic acid anilide dihydrochloride was prepared by reaction of β -chloroacetylenesulfochloride hydrate with aniline.

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INTERACTION OF ACYLOXYDICHORO-1,4-BENZOQUINONES WITH AMINES

A. N. Makarova, M. P. Gribkova, and A. Ya. Berlin

Institute of Experimental and Clinical Oncology of the

Academy of Medical Sciences of the USSR

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It is well known that the most typical reactions of benzoquinones, as derivatives of dihydrobenzene, are addition reactions. However, according to the literature, the reaction of many substituted benzoquinones (such as halo- [1-4], alkoxy- [4-12], phenoxy- [8], hydroxy- [13], amino- [2,8,10,11,14], and thio-1,4-benzoquinones [8]) with amines involves displacement of the substituents in the original molecules by amine residues with formation, as a rule, of derivatives of diamino-1,4-benzoquinone. Reports have also been published [9,12,15] about the synthesis of derivatives of tri- and tetraamino-1,4-benzoquinones.

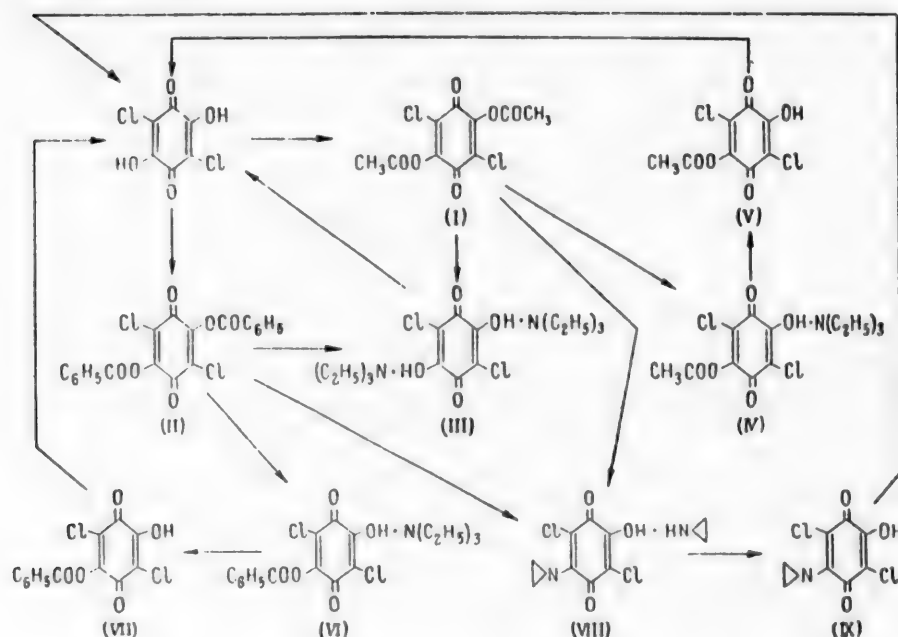
Substituents in the para-position to one another are most easily and smoothly displaced. Quinones containing substituents in the 2,3- and 2,6-positions react with amines very much more slowly and in a more complex fashion [6,10,12]. So far, these reactions have been little studied. The facility with which residues are replaced in the benzoquinone molecule by amines also depends on the nature of the residues. Most easily replaced are amino, alkoxy, phenoxy, and thio groups. Chlorine atoms are replaced with rather more difficulty. No work appears to have been published on interaction of acyloxybenzoquinones with amines.

In the present work we studied the reactions of 2,5-diacetoxy- and 2,5-dibenzoyloxy-3,6-dichloro-1,4-benzoquinones with ethylenimine. The 2,5-diacetoxy-3,6-dichloro-1,4-benzoquinone (I) required for the work was prepared in good yield from chloranilic acid and acetic anhydride; 2,5-dibenzoyloxy-3,6-dichloro-1,4-benzoquinone (II) was obtained in quantitative yield from chloranilic acid and benzoyl chloride.

Reaction of (I) and (II) with ethylenimine in benzene in presence of triethylamine gave the same substance in both cases with a composition (judging by its analysis and properties) corresponding to the bis-triethylammonium salt of 2,5-dihydroxy-3,6-dichloro-1,4-benzoquinone (III). Acidification of the aqueous solution of (III) with dilute hydrochloric acid led to separation of chloranilic acid (see scheme on following page).

Only one of the two amines (triethylamine) participated in the formation of the product (III) of these reactions. In later experiments we therefore reacted (I) and (II) with triethylamine and ethylenimine separately. It was then found that the acyloxy groups of (I) and (II) react less easily with triethylamine alone than in presence of ethylenimine. Reaction of triethylamine with (I) gave the triethylammonium salt of 2-acetoxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (IV) in the form of dark violet crystals. Acidification of an aqueous solution of

*Original Russian pagination. See C.B. translation.



the salt with dilute hydrochloric acid led to immediate separation of bright yellow crystals of 2-acetoxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (V). Similarly, reaction of triethylamine with (II) gave the triethylammonium salt of 2-benzoyloxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (VI). In this case, the reaction is very much slower than that of (I). Acidification of the aqueous solution of (VI) yielded yellow crystals of 2-benzoyloxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (VII). Crystals of chloranilic acid came down from the filtrates, after separation of (VI) and (VII) on lengthy standing.

Reaction of both (I) and (II) with excess of ethyleneimine in anhydrous benzene gave the same substance in the form of violet crystals. Judging by the analysis and properties, it is the ethyleneimmonium salt of 2-ethyleneimino-5-hydroxy-3,6-dichloro-1,4-benzoquinone (VIII). It should be noted that the reaction of ethyleneimine with (I), just like that with triethylamine, goes faster and with better yield than in the case of (II). Acidification of the aqueous solution of (VIII) with dilute hydrochloric acid led to separation of dark-violet crystals of 2-ethyleneimino-5-hydroxy-3,6-dichloro-1,4-benzoquinone (IX). Chloranilic acid came down from the filtrate from separation of (IX) after prolonged standing. The structure of (VIII) and (IX) was confirmed by their similarity to the ammonium salt of 2-amino-5-hydroxy-3,6-dichloro-1,4-benzoquinone - obtained by Erdmann [16] by dissolving chloranil in aqueous ammonia - and to free 2-amino-5-hydroxy-3,6-dichloro-1,4-benzoquinone, which was isolated from the ammonium salt by treatment with hydrochloric acid.

The results show that acyloxydichloro-1,4-benzoquinones, unlike other substituted quinones, react with ethyleneimine with complete replacement of only one acyloxy group. Under the same conditions, chlorine atoms are not replaced by ethyleneimine residues.

EXPERIMENTAL

2,5-Diacetoxy-3,6-dichloro-1,4-benzoquinone (I). A suspension of 1.2 g of chloranilic acid in 5.4 ml of acetic anhydride was boiled for 5 min. The acid went into solution and a yellow precipitate came down on cooling. The latter was filtered and washed with ethanol and ether. Yield 1.45 g (87%). Lemon-yellow crystals with m.p. 183-184° (from benzene). Literature [17]: m.p. 182.5°.

2,5-Dibenzoyloxy-3,6-dichloro-1,4-benzoquinone (II). A suspension of 2 g of chloranilic acid in 9 ml of benzoyl chloride was boiled for 15 min until solution was complete. Yellow crystals came down on cooling. The precipitate was filtered and washed with ethanol and ether. Yield 4 g (quantitative). Bright-yellow crystals with m.p. 212-214° (from benzene).

Found %: C 57.69; H 2.73; Cl 17.10. $C_{20}H_{10}O_6Cl_2$. Calculated %: C 57.55; H 2.40; Cl 17.10.

Bis-triethylammonium salt of 2,5-dihydroxy-3,6-dichloro-1,4-benzoquinone (III). a) From 2,5-diacetoxy-3,6-dichloro-1,4-benzoquinone (I). To a solution of 0.7 g of (I) in 45 ml of dry benzene (cooled with iced water) was added a mixture of 0.25 ml of ethyleneimine and 0.7 ml of triethylamine in 5 ml of benzene, and the mass was vigorously shaken. The color of the solution quickly changed from light yellow through dark red to violet. After 15-min standing in cold water, the liquid began to deposit fine, dark-lilac crystals. Yield 0.12 g (12%). Recrystallization from a mixture of chloroform and methanol (1:1) and two reprecipitations from solution in chloroform gave dark-blue crystals with m.p. 181-182°.

Found %: C 52.21; H 7.56; N 6.37; Cl 16.98. $C_{18}H_{12}O_4N_2Cl_2$. Calculated %: C 52.55; H 7.78; N 6.81; Cl 17.27.

Readily soluble in water, chloroform, acetone, and ethyl acetate.

b) From 2,5-dibenzoyloxy-3,6-dichloro-1,4-benzoquinone (II). To a solution of 0.4 g of (II) in 80 ml of dry benzene, cooled with iced water, was added a mixture of 0.1 g of ethyleneimine and 0.3 ml of triethylamine in 5 ml of benzene; the mass was shaken. The color of the solution changed to dark red. After the mass had stood for 30 min in cold water, it started to deposit a light-lilac precipitate. The mixture was stood overnight in a refrigerator. Yield 0.06 g (15%). Recrystallization from a mixture of chloroform and methanol (1:1) and reprecipitation from chloroform with ether gave pink to lilac crystals with m.p. 181-182°. No depression in a mixed-melting test with the product from a.

Acidification of an aqueous solution of 0.05 g of salt (III) with 5% hydrochloric acid led to immediate separation of lustrous, orange crystals of chloranilic acid. Yield 0.03 g (quantitative); m.p. 285° (decomp.). No depression in a mixed-melting test with authentic chloranilic acid.

Triethylammonium salt of 2-acetoxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (IV). To a solution of 0.07 g of (I) in 4.5 ml of dry benzene was added 0.07 ml of triethylamine, and the mixture was shaken. The color at once changed to red-violet. The mixture was left overnight. A black-violet, coarsely crystalline precipitate came down. Yield 0.05 g (59.5%). M.p. 123-124° (from benzene).

Found %: C 47.90; H 5.42; N 3.94; Cl 19.40. $C_{14}H_9O_5NCl_2$. Calculated %: C 47.72; H 5.40; N 3.97; Cl 20.17.

Readily soluble in water, soluble in benzene and other organic solvents.

2-Acetoxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (V). Into a solution of 0.3 g of (IV) in 25 ml of water was run dropwise 5% hydrochloric acid until the liquid had a strongly acid reaction. Golden-yellow scales at once came down and were quickly filtered, washed with acidified water, and dried in a vacuum desiccator. Yield 0.18 g (80%). Yellow, rectangular plates (under the microscope). M.p. 225° (from benzene, with decomp.).

Found %: C 38.10; H 1.69; Cl 28.10. $C_8H_4O_5Cl_2$. Calculated %: C 38.05; H 1.59; Cl 28.28.

Soluble in ethanol, ether, and benzene. Chloranilic acid comes down from the aqueous acidic filtrate after prolonged standing at room temperature.

Triethylammonium salt of 2-benzoyloxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (VI). To a solution of 0.12 g of (II) in 20 ml of dry benzene was added 0.09 ml of triethylamine, and the mixture allowed to stand at room temperature for 2 days. The mixture gradually acquired a deep-violet color and deposited dark-violet crystals. The solution was evaporated to a small volume. Yield 0.05 g (50%), m.p. 122-123° (from benzene).

Found %: C 55.04; H 5.01; N 3.60; Cl 16.38. $C_{15}H_{11}O_5NCl_2$. Calculated %: C 55.07; H 5.07; N 3.37; Cl 17.15.

Less soluble in water than (IV).

2-Benzoyloxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone (VII). To an aqueous solution of 0.2 g of (VI) was added 5% hydrochloric acid dropwise until the liquid had a strongly acidic reaction. A voluminous precipitate

* All analyses carried out in the analytical laboratory of the Institute under the direction of A. D. Chirayeva.

at once came down and was filtered, washed with acidified water, and dried in a vacuum desiccator. Yield 0.1 g (70%). Yellow crystals, decomp. p. 250° (from benzene).

Found %: C 50.07; H 1.88; Cl 22.23. $C_{15}H_6O_5Cl_2$. Calculated %: C 49.84; H 1.91; Cl 22.68.

Chloranilic acid came down from the aqueous acidic solution after lengthy standing at room temperature.

Ethyleneimmonium salt of 2-hydroxy-5-ethyleneimino-3,6-dichloro-1,4-benzoquinone (VIII). a) From 2,5-diacetoxy-3,6-dichloro-1,4-benzoquinone (I). Ethyleneimine (1.5 ml) was run into a solution (cooled with iced water) of 2.1 g of (I) in 150 ml of anhydrous benzene. The color of the solution at once became reddish-violet, and fine, violet-brown crystals came down. The latter were stood and then filtered and washed with benzene. Weight 2.38 g. Recrystallization from chloroform gave 0.8 g (40%); m.p. 140-141° (decomp). (capillary inserted in the apparatus at 136°).

Found %: C 42.79; H 3.67; N 9.70; Cl 26.84. $C_{19}H_{10}O_3N_2Cl_2$. Calculated %: C 43.32; H 3.61; N 10.10; Cl 25.65.

Soluble in water, chloroform, and other organic solvents.

b) From 2,5-dibenzoyloxy-3,6-dichloro-1,4-benzoquinone (II). To a solution of 1 g of (II) in 200 ml of benzene, cooled with iced water, was added 0.5 ml of ethyleneimine. There was obtained 0.67 g of brown-violet precipitate from which, after recrystallization from benzene was isolated 0.3 g (45%); m.p. 140-141° (decomp.). No depression in a mixed-melting test with the substance obtained by method a.

2-Hydroxy-5-ethyleneimino-3,6-dichloro-1,4-benzoquinone (IX). An aqueous solution of (VIII) was acidified with 5% hydrochloric acid until strongly acidic. The color of the solution changed from violet to cherry-red. After 15 min, a dark violet precipitate came down; m.p. 179-180° (from acetone, decomp.).

Found %: C 41.26; H 2.34; Cl 29.36. $C_8H_5O_3NCl_2$. Calculated %: C 41.02; H 2.13; Cl 30.34.

Soluble in water, readily soluble in acetone, chloroform, methanol, ethanol, and benzene. After standing for a long period, the aqueous filtrate deposited red-orange crystals of chloranilic acid.

SUMMARY

1. The reactions of 2,5-acetoxy- and 2,5-dibenzoyloxy-3,6-dichloro-1,4-benzoquinone with ethyleneimine and triethylamine were studied.

2. Triethylammonium salts of the following were prepared: 2,5-dihydroxy-3,6-dichloro-1,4-benzoquinone; 2-acetoxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone; 2-benzoyloxy-5-hydroxy-3,6-dichloro-1,4-benzoquinone; also, the ethyleneimmonium salt of 2-hydroxy-5-ethyleneimino-3,6-dichloro-1,4-benzoquinone, and the corresponding free hydroxy compounds.

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INTERACTION OF ETHOXYCHLOROQUINONES WITH AMINES

II. REACTIONS OF MONOETHOXYTRICHLORO-1,4-BENZOQUINONE

A. Ya. Berlin and A. N. Makarova

Institute of Experimental and Clinical Oncology,

Academy of Medical Sciences of the USSR

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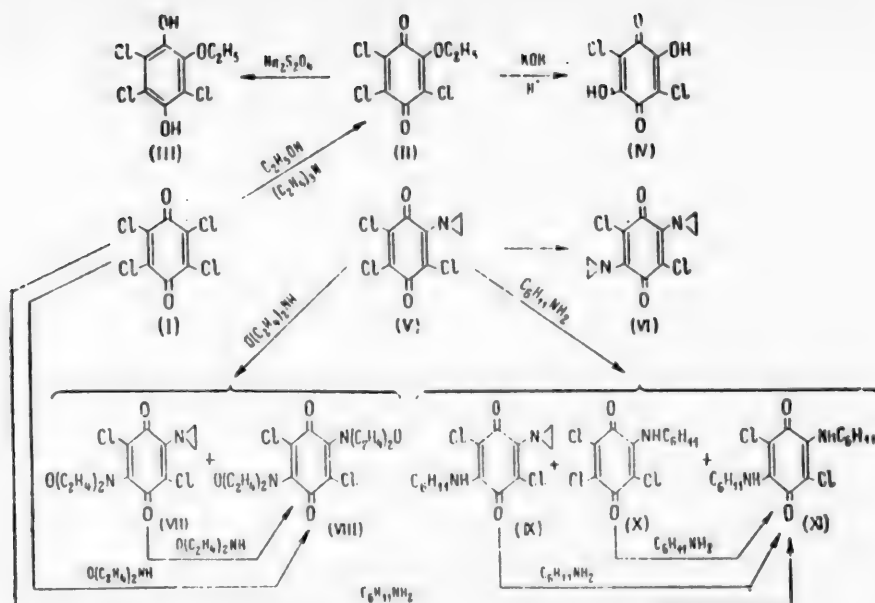
In the present work we describe the preparation of monoethoxytrichlorobenzoquinone and some of its reactions, including reaction with amines. Monoethoxytrichlorobenzoquinone (II) [1] is prepared by reaction of chloranil (I) with ethyl alcohol in presence of triethylamine, with the chloranil and triethylamine in a definite molar ratio. It forms small, lustrous, yellow-orange flakes. Monoethoxytrichlorobenzoquinone is easily reduced by sodium hydrosulfite to monoethoxytrichlorohydroquinone (III). Treatment of the quinone (II) with potassium hydroxide solution at room temperature gives the potassium salt of chloranilic acid, from which the free acid (IV) is obtained by treatment with dilute hydrochloric acid.

Reaction of monoethoxytrichlorobenzoquinone with ethyleneimine led to synthesis of monoethyleneimino-trichloro-1,4-benzoquinone (V) in the form of lustrous, dark cherry-red flakes. Ethyleneiminotrichloroquinone reacts with great facility with a second molecule of ethyleneimine to form the known 2,5-dichloro-3,6-diethyleneimino-1,4-benzoquinone (VI) [2]. It was therefore necessary to remove (V) from the reaction mixture as fast as it was formed. Interaction of quinones with amines usually gives 2,5-diaminoquinones. Only in isolated cases have monoaminoquinones been described [3,4]; however, the only representative of this class with an ethyleneimine residue so far known has been ethyleneiminoxyloquinone [5].** (See scheme on following page.)

Ethyleneiminotrichloroquinone readily reacts with amines. With morpholine it gives, depending on the reaction conditions, 2,5-dichloro-3-ethyleneimino-6-morpholino-1,4-benzoquinone (VII) or 2,5-dichloro-3,6-dimorpholino-1,4-benzoquinone (VIII), or even both substances together. 2,5-Dichloro-3,6-dimorpholino-1,4-benzoquinone is also formed when (VII) or (V) are heated with morpholine. Quinone (V) reacts with still greater facility, but in a more complex manner, with cyclohexylamine. The products are 2,5-dichloro-3-ethyleneimino-6-cyclohexylamino-1,4-benzoquinone (IX), cyclohexylaminotrichloro-1,4-benzoquinone (X), and 2,5-dichloro-3,6-dicyclohexylamino-1,4-benzoquinone (XI) [7]. The quantitative ratio of these products depends on the reaction conditions. With an excess of cyclohexylamine, both (IX) and (X) are converted to quinone (XI) in substantially quantitative yield.

* See C.B. translation.

** After our experimental work had been completed, a paper appeared [6] which reported the preparation of 2-methoxy-5-ethyleneimino-1,4-benzoquinone.



It appears from the above reactions that the interaction of ethoxytrichloroquinone with ethylenimine proceeds in two steps. The ethoxy group is first displaced by the ethylenimine residue with formation of (V). The chlorine atom in the para-position to the ethylenimino group is then replaced by a second ethylenimino group with formation of (VI). Reaction of ethyleniminotrichloroquinone with morpholine likewise goes in two steps, but in another direction. At first the morpholine residue replaces the chlorine in the para-position to the ethylenimino group of the quinone with formation of (VII). Then the second morpholine molecule displaces the ethylenimino residue with formation of (VIII). Acceleration of the second step requires an excess of morpholine or heating of the reaction mixture. Interaction of (V) with cyclohexylamine under the conditions described goes simultaneously in both directions. A cyclohexylamine residue replaces the chlorine in the para-position to the ethylenimino group of the quinone with formation of (IX). At the same time, a cyclohexylamine residue replaces the ethylenimino group with formation of (X). In both cases, a second molecule of cyclohexylamine then enters into reaction and the symmetrical quinone (XI) is formed. Consequently, all of the reactions that we studied proceed in two steps, but in different directions, depending on the nature of the substituents in the quinone molecule and on the properties of the starting amine.

EXPERIMENTAL

Monoethoxytrichloro-1,4-benzoquinone (II). A suspension of 1 g of finely pulverized chloranil in a mixture of 15 ml of ethanol and 0.3 ml of triethylamine was heated on a water bath (80°) for 15 min. The greater part of the quinone went into solution (dark green in color). The liquid was filtered off from unreacted chloranil and the filtrate evaporated to dryness in vacuo. The residue was extracted with ligroine from which 0.4 g of precipitate came down. M.p. 98-99° (from alcohol). Yellow-orange flakes.

Found %: C 37.76; H 1.94; Cl 41.53. $\text{C}_8\text{H}_5\text{O}_3\text{Cl}_3$. Calculated %: C 37.60; H 1.91; Cl 41.64.

Insoluble in water, highly soluble in alcohols, ether, hexane, and other organic solvents.

The potassium salt of chloranilic acid came down as dark-red prisms when potassium hydroxide solution was added to monoethoxytrichlorobenzoquinone. Addition of aqueous 1:1 hydrochloric acid to the aqueous solution of the potassium salt led to separation of chloranilic acid (IV) in the form of light-red, lustrous flakes. M.p. 280-281° (decomp.).

Monoethoxytrichlorohydroquinone (III). To a gently heated suspension of ethoxytrichloroquinone in water was added sodium hydrosulfite until a colorless precipitate formed. The mixture was extracted with ether. After the ethereal solution had been dried, it was evaporated to dryness and the residue recrystallized. M.p. 127-128° (from 1:1 alcohol-water).

Found %: C 37.10; H 2.95. $C_8H_7O_3Cl_3$. Calculated %: C 37.31; H 2.74.

Monoethyleimineotrichloro-1,4-benzoquinone (V). To a solution of 0.2 g of monoethoxytrichloroquinone in 40 ml of alcohol (cooled with iced water) was added 0.04 ml of ethyleneimine. The solution turned dark red. After about a minute, a solid came down and was quickly filtered. Yield 0.15 g (75%). Lustrous, dark-cherry plates. M.p. 185-186° (from alcohol).

Found %: C 37.87; H 1.70; N 5.37; Cl 41.87. $C_8H_4O_2NCl_3$. Calculated %: C 38.05; H 1.60; N 5.54; Cl 42.14.

Crystals continued to come down from the filtrate, at first as a mixture of ethyleneimineotrichloroquinone (V) with a little of the very much less soluble 2,5-dichloro-3,6-diethyleiminobenzoquinone (VI) [2], and later as a mixture whose predominant component was (VI), and, finally, as pure (VI).

Reaction of monoethyleimineotrichloroquinone (V) with morpholine. a) To a suspension of 0.1 g of (V) in 25 ml of methanol was added 0.03 ml of morpholine. The color of the solution changed from red to dark cherry, and the precipitate gradually disappeared. The reaction mixture was left overnight at room temperature. The resulting dark-green precipitate of (VII) (0.04 g) was filtered off. Evaporation of the solution to a small volume led to separation of another 0.04 g of (VII). Total yield 0.08 g (70%). Dark-green plates. M.p. 143-144° (from alcohol).

Found %: C 47.47; H 4.28; N 9.35. $C_{12}H_{12}O_3N_2Cl_2$. Calculated %: C 47.53; H 4.02; N 9.24.

b) To a suspension of 0.1 g of (V) in 20 ml of methanol was added 0.2 ml (5 mole) of morpholine and 0.05 ml of triethylamine. The color changed to dark cherry. After 25 min, a lustrous, dark-green precipitate of 2,5-dichloro-3-ethyleiminino-6-morpholinobenzoquinone (VII) came down. Yield 0.08 g (70%). The evaporated and cooled filtrate deposited 0.02 g of (VIII) in the form of a yellow-brown precipitate.

Lustrous, yellow-brown plates. M.p. 202-203° (from alcohol). A mixture with 2,5-dichloro-3,6-dimorpholinobenzoquinone obtained from chloranil and morpholine [6] melted unchanged.

Heating of 0.1 g of (VII) with 3 ml of methanol and 0.1 ml of morpholine to the boil for an hour gave 2,5-dichloro-3,6-dimorpholinobenzoquinone. Yield 0.09 g (70%).

The same result was obtained when ethyleneimineotrichloroquinone (V) was heated with excess of morpholine.

Reaction of monoethyleimineotrichlorobenzoquinone (V) with cyclohexylamine. A solution of 0.1 g of (V) in 75 ml of methanol, 0.05 ml of cyclohexylamine, and 0.05 ml of triethylamine was stood for 24 hr in a refrigerator. A pink precipitate formed. Yield 0.04 g. No melting-point depression in a mixed-melting test with authentic 2,5-dichloro-3,6-dicyclohexylaminobenzoquinone (XI) [7]. The filtrate was evaporated to dryness in vacuo. Fractional crystallization of the residue from alcohol gave 0.03 g of 2,5-dichloro-3-ethyleiminino-6-cyclohexylamino-1,4-benzoquinone (IX) in the form of lustrous, yellow-brown plates; m.p. 185-186°.

Found %: C 53.01; H 4.84. $C_{14}H_{16}O_2N_2Cl_2$. Calculated %: C 53.33; H 5.12.

The next crop of crystals was 0.02 g of trichlorocyclohexylamino-1,4-benzoquinone (X) in the form of dark-cherry prisms; m.p. 125-126°.

Found %: C 46.31; H 3.66. $C_{12}H_{12}O_2NCl_3$. Calculated %: C 46.69; H 3.92.

Addition of cyclohexylamine at room temperature to an alcoholic solution of (IX) or (X) gave 2,5-dichloro-3,6-dicyclohexylamino-1,4-benzoquinone (XI).

SUMMARY

1. It was established that reaction of chloranil with alcohol in presence of triethylamine gave monoethoxytrichloro-1,4-benzoquinone.
2. Reaction of monoethoxytrichloro-1,4-benzoquinone with ethyleneimine gave monoethyleimineotrichloro-1,4-benzoquinone and 2,5-diethyleiminino-3,6-dichloro-1,4-benzoquinone.
3. Reaction of monoethyleimineotrichloro-1,4-benzoquinone with morpholine gave 2,5-dichloro-3-ethyleiminino-6-morpholino-1,4-benzoquinone and 2,5-dichloro-3,6-dimorpholino-1,4-benzoquinone.

4. Reaction of monoethyleneiminotrichloro-1,4-benzoquinone with cyclohexylamine gave 2,5-dichloro-3-ethyleneimino-6-cyclohexylamino-1,4-benzoquinone, trichlorocyclohexylamino-1,4-benzoquinone, and 2,5-dichloro-3,6-dicyclohexylamino-1,4-benzoquinone.

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SYNTHESIS OF THIAZOLE DERIVATIVES

XV. BENZOTHAZOLYLPYRAZOLONES

V. M. Zubarovskii and G. P. Khodot

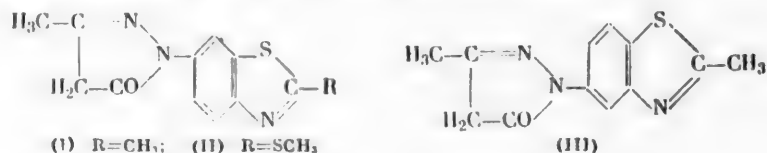
Institute of Organic Chemistry, Academy of Sciences of the UkrSSR

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The recently described 2-methyl-(6-benzothiazolyl)-, 2-methyl-(5-benzothiazolyl)-, and 2-methylmercapto-(6-benzothiazolyl)-hydrazines** were used in the present work for synthesis of new benzothiazolylpyrazolones (I-III), which can be utilized for the preparation of various polymethine dyes. It was also a matter of interest to investigate the antitubercular properties of benzothiazolylpyrazolones.



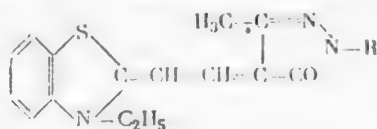
The 2-methyl-(6-benzothiazolyl)- and 2-methyl-(5-benzothiazolyl)-hydrazines needed for the work are unstable and were therefore prepared in the form of their hydrochlorides, from which the bases were liberated as needed. 2-Methylmercapto-(6-benzothiazolyl)-hydrazine can be kept for a considerable time, even in the form of the base. Benzothiazolylpyrazolones were synthesized by condensation of the hydrazines with ethyl acetoacetate. Performance of the condensation without heating leads to formation of benzothiazolylhydrazones of ethyl acetoacetate, which split off alcohol when melted and are converted to pyrazolones. For preparation of the latter, a mixture of benzothiazolylhydrazine and ethyl acetoacetate was heated to 130-135° in order to eliminate the water and alcohol formed by the condensation. Benzothiazolylpyrazolones are obtained in yields of 80-90%; they are easily purified by precipitation from alkali solution and by crystallization. They are colorless, crystalline substances of amphoteric character; addition of ferric chloride to their aqueous alcoholic solution imparts a brown-red color which quickly disappears.

Benzothiazolylpyrazolones, in particular, compound (I), possess slight antitubercular activity.

*Original Russian pagination. See C.B. translation.

See *Zhur. Obshch. Khim.*, **26, 797 (1956).

The active methylene group of the pyrazolone ring of benzothiazolypyrazolones enables them to enter into various condensation reactions, for example with aldehydes, p-nitrosodimethylaniline, diphenylformamidine, and 2-(ω -acetanilidovinyl)-benzothiazole ethiodide. With the last-named compound, in a medium of pyridine, benzothiazolypyrazolones form dyes — dimethinemerocyanines (IV-VI).

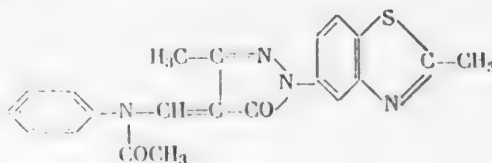


(IV) R = 2-methyl-6-benzothiazolyl-;

(V) R = 2-methylmercapto-6-benzothiazolyl-;

(VI) R = 2-methyl-5-benzothiazolyl-;

(VII) R = phenyl-.



(VIII)

A secondary product accompanying the merocyanines in each case is the known symmetrical cyanine dye, bis-(3-ethyl-2-benzothiazol)trimethinemerocyanine iodide, as well as various yellow substances of unknown structure. The merocyanines are easily purified from these admixtures by chromatography. By this technique the yellow substances can be separated in crystalline form. The latter are formed both when equimolar quantities of benzothiazolypyrazolone and 2-(ω -acetanilidovinyl)-benzothiazole ethiodide are used, and when the former is in excess. They are products of a reaction proceeding side by side with formation of the merocyanine, and evidently associated with transformation of 2-(ω -acetanilidovinyl)-benzothiazole into a symmetrical thiacyanocyanine. We consider that the yellow substance obtained by condensation of (III) with 2-(ω -acetanilidovinyl)-benzothiazole ethiodide, with m.p. 270° and λ_{\max} 415 m μ , possesses the structure of (VIII).

The other two yellow substances separated in the synthesis of merocyanines (V) and (VI) must have analogous structures.

Merocyanines (IV-VI) are easily decolorized by hydrochloric acid. On heating with dimethyl sulfate they form salts (possessing an active methyl group) which can be used for preparation of complex polymethine dyes.

EXPERIMENTAL

Hydrochlorides of benzothiazolylhydrazines. Unpurified 2-methyl-(6-benzothiazolyl)-hydrazine, prepared from 9.84 g of 2-methyl-6-aminobenzothiazole,* was dissolved in 50 ml of dilute (1:2) HCl, thrice decolorized with carbon at 50°, and heated in a porcelain dish on a water bath until nearly the whole of the liquid had evaporated and a clot of viscous mass had formed. To the residue was added 25 ml of anhydrous alcohol, and the salt was thoroughly triturated with the alcohol, filtered, and washed with ether. Yield of salt 8.0 g; pinkish-white crystals with m.p. 232° (decomp.). The salt (6 g) was dissolved in water (40 ml) and 25% ammonia (10 ml) was stirred in quickly. After the mixture had been cooled in ice, the precipitate was filtered, washed with water, thoroughly suction filtered, and crystallized from 100 ml of xylene. A layer of water formed and was separated in a previously heated funnel. The transparent, yellow xylene solution was cooled with water, and the precipitate was filtered and washed with ligroine. Yield 3.5 g; yellowish-white needles with m.p. 143°. The free base was quickly used for synthesis of the pyrazolone.

2-Methyl-(5-benzothiazolyl)-hydrazine hydrochloride was similarly prepared. M.p. 240° (decomp.). The hydrazine base, precipitated by ammonia from 6 g of salt and washed with water, crystallized. The separated hydrazine base was filtered off and washed with a small quantity of cooled alcohol. Yield 3.5-3.6 g; m.p. 158° (from alcohol). Unlike the preceding base, it can be kept for 1-2 days.

(2-Methyl-6-benzothiazolyl)-hydrazone of ethyl acetoacetate. To 0.9 g (0.005 mole) of (2-methylbenzothiazolyl)-hydrazine was added 0.65 g (0.005 mole) of ethyl acetoacetate with stirring. Slight heat was developed. The viscous, oily liquid was stood for 15 hr and then triturated with excess of ligroine, filtered, and washed on the filter with the same solvent. Yield 0.9 g (75%); colorless needles with m.p. 95-98° (decomp.) (from ligroine with b.p. 100-120°).

Found %: N 14.26, 14.29; S 11.07, 11.23. $C_{14}H_{17}O_2N_3S$. Calculated %: N 14.13; S 11.00.

No coloration in aqueous alcoholic solution with $FeCl_3$. At 140-160° it changes into a product identical with benzothiazolypyrazolone.

* Zhur, Obshch. Khim. 26, 797 (1956).

Hydrazones are similarly formed from the other benzothiazolylhydrazines and ethyl acetoacetate.

1-(2'-Methyl-6'-benzothiazolyl)-3-methyl-5-pyrazolone (I). 3.0 g (0.0152 mole) of (2-methyl-6-benzothiazolyl)-hydrazine (recrystallized from xylene) was stirred with 2.05 g (0.0158 mole) of freshly distilled ethyl acetoacetate. The temperature of the mixture rose to 45-50°. The temperature was raised to 130-135°, and the mixture stirred for 25 min. The alcohol and water were gradually boiled off from the transparent yellow liquid. Removal of the alcohol was accompanied by frothing, which ceased toward the close of heating; at this stage the mass usually solidified. The solid product was crushed to powder, mixed with dry ether, filtered, and washed with ether. Yield 3.4 g (91.2%); pale-yellow crystals.

A solution of 20 g of crude pyrazolone in 200 ml of 2.5% NaOH solution was prepared at 50°; the hot solution was filtered at 50° and treated three times with carbon at the same temperature. The filtrate was cooled in iced water, and dilute HCl (1:3) was gradually added until the mixture had a pH of 5. The precipitate was filtered, washed with water, and crystallized from 100 ml of methanol. The mother liquor was decolorized with carbon. The filtrate was cooled in ice, and the finely crystalline, colorless precipitate was filtered and washed with dry ether. Yield 14 g of (I) with m.p. 175° (from methanol).

Found %: N 16.97, 16.91. $C_{12}H_{11}ON_3S$. Calculated %: N 17.14.

The amphoteric product is soluble in dilute HCl, soluble in benzene and many other organic solvents, insoluble in ligroine. The aqueous alcoholic solution turns brown-red when $FeCl_3$ solution is added; the color gradually disappears. Excess of $FeCl_3$ leads to separation of a light-colored precipitate.

Boiling of a solution of equimolar amounts of benzaldehyde and (I) in pyridine for 30 min led to formation of the benzylidene derivative which came down on addition of water; fine, reddish-orange crystals with m.p. 156° (from methanol).

Found %: N 12.60, 12.71. $C_{19}H_{15}ON_3S$. Calculated %: S 8.49.

Heating of equimolar quantities of p-nitrosodimethylaniline and (I) in pyridine for 1.5 hr (paraffin wax bath at 140°) gave a violet-red dye - 1-(2'-methyl-6'-benzothiazolyl)-3-methyl-4-(p-dimethylaminophenylimino)-5-pyrazolone - which was precipitated by water, and purified by chromatography on Al_2O_3 from $CHCl_3$, and by crystallization from xylene. Yield 40%. Fine, violet crystals with m.p. 243°, λ_{max} 526 m μ (in alcohol).

Found %: S 8.33, 8.22. $C_{20}H_{19}ON_5S$. Calculated %: S 8.49.

1-(2'-Methyl-5'-benzothiazolyl)-3-methyl-5-pyrazolone (III). 2.96 g of freshly prepared (2-methyl-5-benzothiazolyl)-hydrazine was similarly condensed with 2.05 g (2 ml) of ethyl acetoacetate. Yield 3.2 g. The pyrazolone was precipitated by dilute HCl from its cooled alkaline solution in the form of a viscous oil which gradually solidified. The precipitate was crystallized from 450 ml of methanol; the mother liquor was twice decolorized with carbon (2.5 g each time), and the filtrate was cooled in ice. The precipitate was washed with dry ether. Colorless crystals with m.p. 194° (from alcohol).

Found %: N 16.93, 16.83. $C_{12}H_{11}ON_3S$. Calculated %: N 17.14.

The product gave a brown-red coloration with $FeCl_3$ in aqueous alcoholic solution.

Benzylidene derivative: reddish-orange crystals with m.p. 164° (from methanol).

Found %: N 12.44, 12.23. $C_{19}H_{15}ON_3S$. Calculated %: N 12.61.

Boiling of a mixture of 1.47 g (0.0075 mole) of diphenylformamidine, 1.86 g (0.0075 mole) of (III), and 6 ml of dry pyridine for 45 min gave 1-(2'-methyl-5'-benzothiazolo)-3-methyl-4-(phenylaminomethylene)-5-pyrazolone, which came out on addition of an equal amount of water to the hot solution. Yield 2.6 g (nearly theoretical). Light-yellow needles with m.p. 214° (from benzene).

Found %: S 9.11, 9.09. $C_{19}H_{16}ON_4S$. Calculated %: S 9.19.

1-(2'-Methyl-6'-mercaptobenzothiazolyl)-3-methyl-5-pyrazolone (II). Synthesized from 3.2 g of (2-methyl-6-mercaptobenzothiazolyl)-hydrazine and 1.95 g of ethyl acetoacetate. Yield 3.3 g (79%). Pyrazolone (II) was purified by precipitation with dilute (1:3) HCl from solution in 65 ml of 5% NaOH solution, and crystallized from 100 ml of methanol in presence of carbon. Colorless crystals with m.p. 187°.

Found %: N 14.87, 14.77. $C_{12}H_{11}ON_3S_2$. Calculated %: N 14.81.

Benzylidene derivative: small, orange-red needles with m.p. 171° (from methanol).

Found %: N 11.42, 11.36. $C_{19}H_{15}ON_3S_2$. Calculated %: N 11.51.

1-(2'-Methyl-6'-benzothiazolyl)-3-methyl-4-(3"-ethylbenzothiazolinyldene-2"-ethylidene)-5-pyrazolone (IV). A mixture of 2.75 g (0.0113 mole) of pyrazolone (I), 3.4 g (0.0075 mole) of 2-(ω -acetanilidovinyl)-benzothiazole ethiodide and 6 ml of dry pyridine was heated to give a dark-red solution which was then boiled for 45 min. After 3 hr, the precipitate was filtered and washed many times with hot methanol and dry ether. The crude merocyanine consisted of an orange-red, finely crystalline powder. Yield 3.0-3.2 g. Excess of dry ether was added to the filtrate to bring down a pale-violet, crystalline precipitate (1.3 g) which was dissolved in 30 ml of alcohol. The solution was stood for 15 hr. Bluish-gray crystals with a metallic luster came out (0.15 g) and were filtered and washed with alcohol; λ_{\max} 559 m μ (in alcohol), identical with the λ_{\max} of the symmetrical cyanine dye 3,3'-diethylthiacarbocyanine iodide; the two dyes also possess identical light-absorption curves. The alcoholic solution remaining after crystallization of the thiacarbocyanine was decolorized with carbon and mixed with excess of dry ether. The precipitated white crystals consisted of a substance (0.7 g) with m.p. 146-147° [a mixture with (2-methyl-6-benzothiazolyl)-hydrazine melted at the same temperature]. The merocyanine was dissolved in $CHCl_3$ and chromatographed on Al_2O_3 to form two clearly demarcated zones: The lower, red zone contained the synthesized dye (IV); the upper, yellow zone contained impurity. Three zones were obtained if the crude merocyanine, prior to chromatographic treatment, was inadequately washed with warm methanol; in this event, the topmost zone (violet-red) contained the symmetrical thiacarbocyanine. Dye (IV) was eluted with $CHCl_3$, and the yellow zone was transferred to a fresh adsorption column and eluted with a 4:1 mixture of $CHCl_3$ and alcohol. The solvents were completely removed from the eluates to leave 1.96 g (40.1%) of red dye (IV) and 0.45 g of a yellow, finely crystalline substance. (IV) was in the form of lustrous, red scales with m.p. 245° (from xylene) * and λ_{\max} 492 m μ (in alcohol).

Found %: N 13.14, 13.13. $C_{23}H_{20}ON_4S_2$. Calculated %: N 12.96.

After further chromatographic treatment and crystallization, the yellow substance had m.p. 275° (from benzene), and λ_{\max} 417 m μ (in alcohol).

1-(2'-Methyl-5'-benzothiazolyl)-3-methyl-4-(3"-ethylbenzothiazolinyldene-2"-ethylidene)-5-pyrazolone (VI). A mixture of 1.1 g of pyrazolone (III), 1.35 g of 2-(ω -acetanilidovinyl)-benzothiazole ethiodide, and 3 ml of dry pyridine was heated for 20 min at 120° with periodic stirring. To the cooled reaction products was added 5 ml of methanol; the merocyanine was filtered, mixed with 10 ml of hot alcohol, again filtered, and washed on the filter with alcohol until the violet-red filtrate (containing a trace of symmetrical thiacarbocyanine) became brown-orange; washing could be accelerated if stirring of the dye with hot alcohol and washing with dry ether were repeated. Yield 1.35 g. From the filtrate could be separated, with the help of dry ether, symmetrical thiacarbocyanine with λ_{\max} 559 m μ and a small quantity of unreacted pyrazolone (III).

The merocyanine was dissolved in 250 ml of $CHCl_3$ and chromatographed on Al_2O_3 . The operation led to formation of three zones; The top one contained symmetrical thiacarbocyanine with λ_{\max} 559 m μ , the middle one a yellow impurity, and the bottom one merocyanine (VI). From the middle zone was isolated 0.15 g of (VIII); fine, orange-yellow crystals with m.p. 270° (from benzene), and λ_{\max} 415 m μ (in alcohol).

Found %: N 14.60, 14.41. $C_{21}H_{15}O_2N_4S$. Calculated %: N 14.35.

From the bottom zone was obtained 0.95 g (73%) of merocyanine (VI); fine, red crystals with m.p. 286° (from xylene) and λ_{\max} 492 m μ (in alcohol).

Found %: N 12.90, 12.77. $C_{23}H_{20}ON_4S_2$. Calculated %: N 12.96.

1-(2'-Methyl-6'-mercaptobenzothiazolyl)-3-methyl-4-(3"-ethylbenzothiazolinyldene-2"-ethylidene)-5-pyrazolone (V). A mixture of 0.83 g of pyrazolone (II), 0.9 g of 2-(ω -acetanilidovinyl)-benzothiazole ethiodide, and 2 ml of dry pyridine was heated with gentle boiling for 25 min. After 1.5 hr, 20 ml of alcohol was

* During melting-point determinations on the dyes, the capillary was put into a salt bath with a temperature of 200-220°.

added. The merocyanine was filtered, washed, purified by chromatography, and recrystallized; light-red, fine needles with m.p. 207° (from xylene) and λ_{\max} 492 m μ (in alcohol).

Found %: S 20.57, 20.47. $C_{23}H_{20}ON_4S_3$. Calculated %: S 20.68.

During chromatographic purification of merocyanine (V), there was isolated, apart from the symmetrical thiocarbocyanine, a yellow crystalline substance with m.p. 263° and λ_{\max} 428 m μ (in alcohol).

1-Phenyl-3-methyl-4-(3'-ethylbenzothiazolinyldiene-2'-ethylidene)-5-pyrazolone (VII). Merocyanine (VII) was similarly synthesized for comparison of its properties with those of merocyanines (IV-VI). The symmetrical thiocarbocyanine and a yellow impurity were again detected during chromatographic purification; (VII) has m.p. 211° (from xylene) and λ_{\max} 492 m μ (in alcohol).

Found %: N 11.53, 11.34. $C_{21}H_{19}ON_3S$. Calculated %: N 11.63.

SUMMARY

Condensation of benzothiazolylhydrazines with ethyl acetoacetate gave the previously undescribed benzothiazolylpyrazolones: 1-(2'-methyl-6'-benzothiazolyl)-, 1-(2'-5'-methylbenzothiazolyl)-, and 1-(2'-methyl-6'-mercaptobenzothiazolyl)-3-methyl-5-pyrazolones. The properties of these compounds and their derivatives are described.

DEVELOPMENT OF SYNTHESIS OF ORGANIC COMPOUNDS LABELED WITH THE ISOTOPE N^{15}

B. A. Geller and L. S. Samosvat

L. V. Pisarzhevskii Institute of Physical Chemistry, Academy of Sciences of the USSR

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Syntheses of organic compounds labeled with the heavy nitrogen isotope start from a series of inorganic salts containing N^{15} : ammonium salts, nitrates, nitrites, etc. The presence of N^{15} in these common compounds makes them extremely expensive, and therefore the usual methods of synthesis, which do not allow for the expense involved, often become unsuitable. In this paper, we describe convenient methods of synthesis of typical aromatic nitrogen compounds.*

N^{15} -Benzamide

Of the methods of preparation of N^{15} -benzamide described in the literature, the best results are obtained by the method of Swan and Kelly [2], in which regeneration of ammonium chloride is omitted and the yields of benzamide approximate to theoretical. Of the three solvents tried (chloroform [2], dichloroethane, and benzene), the best yield and quality of benzamide were obtained with benzene. The experimental technique is simplified with benzene because benzamide is very sparingly soluble in it,** and the solvent does not need to be distilled off.

The procedure was as follows. A 2-liter, two-necked, round-bottomed flask fitted with a stirrer was charged with an ice-cooled solution of 12.8 g (0.160 mole) of $N^{15}H_4NO_3$ (or the equivalent quantity of another ammonium salt) in 80 ml of water. The solution was covered with a thin (1-2 mm) layer of benzene and a cooled solution

* Some of the syntheses described here have been briefly reported in [1].

** We determined the solubility of benzamide in benzene and obtained a value approaching 0.14 g in 100 ml of benzene at 20°.

of 13.52 g (0.333 mole) of sodium hydroxide in 60 ml of water was introduced below the surface of the benzene through a funnel with a long end. Rapid addition was then made of a solution of 22.3 g (18.4 ml or 0.159 mole) of benzoyl chloride* in 600 ml of benzene; the mouth of the flask was tightly closed, and the contents vigorously stirred for 1-1.5 hr at room temperature (until the odor of benzoyl chloride had disappeared). The flask was cooled with ice, and both solutions — aqueous and benzene — were filtered together through a Buchner funnel. The precipitate was washed twice with pure, cooled benzene, pressed, and dried in a drying cupboard at 35-90°. The filtrate was separated into its components in a separating funnel. The benzene solution could be used for subsequent syntheses. The aqueous layer was treated 5-6 times with small portions of chloroform for extraction of the N¹⁵-benzamide. The chloroform extract was dried with anhydrous sodium sulfate. The solvent was taken off on a water bath, and the dry residue added to the main mass of N¹⁵-benzamide. Yield 18-18.5 g (93-96%). The melting point of the unrecrystallized product was not lower than 126°. This purity is adequate for the majority of organic syntheses.* *

For utilization of the heavy nitrogen, the aqueous layer from the extraction was made alkaline with 4-5 g of sodium hydroxide, and the ammonia distilled into a receiver containing 12 ml of 1 N hydrochloric acid. Evaporation of the distillate yielded 0.2-0.5 g of ammonium chloride. Taking this recovery into account, the product yield was 97-99%.

N¹⁵-Aniline

Hofmann rearrangement of benzamide for preparation of aniline has not been adequately studied [3]. Preparation of the intermediate product — N-bromo- or N-chlorobenzamide — in a yield of up to 95% has been described [4]. On the basis of these incomplete data, we developed the Hofmann preparation of aniline without isolation of N-bromobenzamide.

Into a 0.5-liter round-bottomed flask fitted with stirrer were charged 20 g of sodium hydroxide in 190 ml of water. The solution was cooled with iced water, and 11 ml of bromine was run in with vigorous stirring in the course of 20-25 min. To the cooled and stirred solution was then added portionwise (in the course of 8-10 min), 20 g of finely pulverized N¹⁵-benzamide. The solution was kept in ice for 20-30 min,** and transferred to a steam-distillation flask; after addition of 11.4 g of sodium hydroxide in 31 ml of water, the solution was refluxed for 40-50 min on a boiling water bath. The condenser was then replaced by a tube with a ground-glass connection, and the aniline was steam distilled. The residue in the flask was acidified with hydrochloric acid until it contained 5% of HCl, boiled for 15 min, and again made alkaline. The aniline was steam distilled. The two distillates were combined. The aniline was extracted with ether (peroxide-free) and dried with solid sodium sulfate. The ether was taken off in the vacuum of a water-jet pump with gentle heating on a water bath. Yield 13.0-13.4 g (84-87%). Refractive index 1.5858-1.5860. Recovery of heavy nitrogen was inexpedient, since it gave only 0.1-0.2 g of N¹⁵-ammonium chloride.

N¹⁵-α-Naphthylamine

The most convenient method of preparation of N¹⁵-α-naphthylamine is that of Calm [6]. The reaction goes in one step if we exclude the hydrolysis of the acetylene derivative performed during separation of aniline. The starting N¹⁵-ammonium chloride is taken in large excess, but is completely and easily regenerated.

A mixture of 7.2 g of anhydrous sodium acetate with 3 g (0.057 mole) of N¹⁵-ammonium chloride and 2.4 g (0.017 mole) of α-naphthol (well pulverized in a mortar) was charged into ampoules (diameter 25 mm, length 250 mm),**** After addition of 3 ml of glacial acetic acid, the ampoule was sealed and heated for 8 to 10 hr at 280°. After cooling, the ampoule was carefully opened (care being taken in view of the residual pressure), the contents washed out with the minimum quantity of water onto a filter, and washed until the reaction for

* The quantity of benzoyl chloride must be strictly maintained as here specified with a deficiency of 0.5-0.7%. Excess of benzoyl chloride remains in the product and cannot be eliminated without losses of the latter.

** We obtained N¹⁵-benzonitrile in about 76% yield by heating N¹⁵-benzamide with a small excess of phosphorus pentoxide (as described in the literature [5], and in analogy with the preparation of acetonitrile).

*** More prolonged standing in ice caused the color of the solution to change from yellow to orange, and then to brick red. The solution also became very turbid and the aniline yield fell sharply.

**** The walls of the ampoule must be not less than 2 mm thick, because pressure builds up during the reaction and fracture is possible.

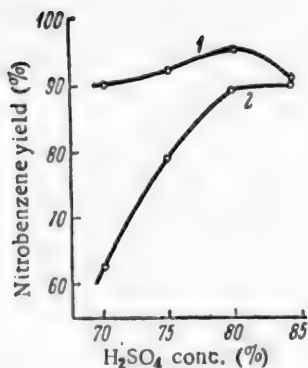


Fig. 1. Influence of sulfuric acid concentration on yield of nitrobenzene. Excess of sulfuric acid per mole of nitrate: 1) 400 ml; 2) 300 ml.

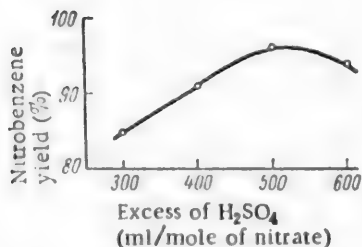


Fig. 2. Influence of quantity of 80% sulfuric acid on yield of nitrobenzene.

amine in the form of light-colored crystals with m.p. 110-113°. Yield about 68%, with allowance for regeneration from aqueous solution, and about 78% with allowance for full regeneration.

Regeneration of N^{15} -ammonium chloride. a) Distillation of ammonia from the first aqueous filtrate gave 1.8-1.9 g of ammonium chloride, which could be directly employed for further syntheses of β -naphthylamine.

b) Synthesis of β -naphthylamine was accompanied by 15-20% conversion to β, β' -dinaphthylamine and resinous admixtures. Kjeldahl treatment of these secondary products led to regeneration of about 0.1 g of ammonium chloride, or 16-20% of the original quantity.

N^{15} -Nitrobenzene

The most convenient synthesis of N^{15} -nitrobenzene is by nitration of benzene.* Nitration of benzene with a mixture of 65% nitric and sulfuric acids [7] gave a yield of nitrobenzene of about 58% (on the nitric acid). High yields of nitrobenzene (about 98%) are possible, as shown by Kobe and Mills [8], by use of the theoretical quantity of 100% nitric acid. However, the preparation of such an acid containing N^{15} is associated with great difficulties and with losses of heavy nitrogen.

* A possible variant of the preparation of nitrobenzene by oxidation of labeled aniline involves three steps with an over-all yield of 60-65%.

chloride ion was negative (filtrate I). The precipitate was refluxed in 100 ml of 1.2% sodium hydroxide solution for 30 min. The flask was cooled in ice, and the precipitate was filtered and washed 2-3 times with iced water (filtrate II). The precipitate was then again refluxed with 100 ml of 6% hydrochloric acid for an hour. The hot solution was filtered (filtrate III). On the filter (washed with water) was retained α, α' -dinaphthylamine and resinous impurity. Filtrate II was treated 3-4 times with ether. The extract, containing a little α -naphthylamine, was combined with filtrate III, which was then made alkaline with 10 g of sodium hydroxide. The ether was distilled off on a water bath, and then the α -naphthylamine was steam distilled. α -Naphthylamine in the distillate was extracted with ether; the extract was dried with solid sodium hydroxide, and the solvent was taken off to leave light-yellow crystals. Yield 1.5-1.6 g (77-82%, allowing for regeneration by method a below, and 90-92%, allowing for complete regeneration).

Regeneration of N^{15} -ammonium chloride. a) Filtrate I was transferred to a flask and made alkaline with 5 g of sodium hydroxide. The ammonia was distilled off with steam into a receiver containing 3 ml of concentrated hydrochloric acid diluted with water. Completion of distillation was detected by a Nessler test. Evaporation of the distillate left 1.65-1.7 g of N^{15} -ammonium chloride.

b) The dinaphthylamine and resinous admixtures were worked up by the Kjeldahl method, and the ammonia distilled off from the reaction mixture into hydrochloric acid. In this way, a further 10% (approx.) of the original heavy nitrogen was recovered.

N^{15} - β -Naphthylamine

For preparation of β -naphthylamine [6], an ampoule was charged with 1.5 g (0.01 mole) of β -naphthol, 2.4 g (0.045 mole) of N^{15} -ammonium chloride, 4.1 g of anhydrous sodium acetate, and 1.5 ml of glacial acetic acid. The reaction mass was worked up by the procedure described for α -naphthylamine to give 1.0-1.1 g of N^{15} - β -naphthyl-

We developed a method of nitration with sodium nitrate and sulfuric acid which gave a yield of up to 96% (on the nitrate). The influence of temperature and of the benzene/sodium nitrate ratio on the yield of product was investigated. The influence of concentration and quantity of sulfuric acid on the yield of nitrobenzene is plotted in Figs. 1 and 2. On the basis of these data, we made use of 500-ml excess of 80% sulfuric acid per mole of nitrate.

The following are the details of our method. Into a round-bottomed, two-necked flask (capacity 0.7 liter), were charged 21.95 g (0.25 mole) of thoroughly pulverized N^{15} -sodium nitrate and 55 ml (0.62 mole) of benzene. With heating on a water bath to 60-62° and good stirring, addition was made through a dropping funnel; in the course of 1 hr, of 135 ml of 80% sulfuric acid. The reactor was heated for another hour at 70-74°. The reaction mass was run into a porcelain beaker (1-liter capacity) and carefully (with cooling) diluted with 200 ml of iced water. The mixture was separated in a separating funnel; the nitrobenzene layer was washed once with water, which was then combined with the acid layer, and the latter was treated three times with benzene for extraction of the dissolved nitrobenzene. The extracts and the nitrobenzene layer were placed in a flask and nearly the whole of the benzene was taken off by heating on a boiling water bath. The nitrobenzene was thereupon distilled with steam* and separated from the aqueous layer in a separating funnel; the aqueous layer was worked up with ether for extraction of residues of nitrobenzene. The ethereal solution and the nitrobenzene were combined and dried with anhydrous sodium sulfate. The ether was taken off on a water bath,** and the benzene in the vacuum of a water-jet pump (approx. 20 mm) at 50-60°. Distillation was continued until the required refractive index of nitrobenzene was obtained — not lower than n_D^{20} 1.5510. Yield 28-29 g (91-94%).

Dinitrobenzene crystallized (in very small amounts: up to 0.5 g) from the residue after steam distillation. Regeneration of nitrogen from it would have been pointless.

Our new method is of interest for nitration of other aromatic hydrocarbons with nitrates,***

SUMMARY

Methods were developed for the preparation of heavy nitrogen-labeled benzamide, aniline, α - and β -naphthylamines and nitrobenzene.

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*The tip of the funnel must reach the middle of the flask in order that the acid should drip into the benzene and not onto the walls of the flask.

**Steam distillation was continued only until drops of nitrobenzene ceased to appear in the receiver (changed 2-3 times).

***Distillation can be speeded up by drawing a current of air through a capillary with the water-jet pump.

****According to the literature, nitration with sodium nitrite in presence of catalysts gives a yield of nitrobenzene of not more than 40% [9].

CATALYTIC SYNTHESIS OF β -ARYLAMINOKETONES

N. S. Kozlov and Z. A. Abramova

Perm Institute of Agriculture

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In preceding papers, one of us described a method of preparation of β -arylamino ketones by catalytic condensation of Schiff bases with fatty-aromatic ketones (1st variant), or of primary aromatic amines with chalcones (2nd variant) [1]. The reaction mechanism has also been studied [2].

The present work is a continuation of the earlier investigations. Starting components were primary aromatic amines - p-ethylaniline, p-aminocymene - and a fatty-aromatic ketone (p-methoxyacetophenone). Using two different methods, we synthesized seven β -arylamino ketones not previously described in the literature. Arylamino ketones (I-VII) (see table) were synthesized by the first variant. Condensation of p-ethylaniline with benzylideneacetophenone gave (I) by the second variant, and condensation of p-aminocymene to give (VII) was also effected by the second variant. The catalyst in both variants of the synthesis was the hydrochloride of the amine brought into condensation, or introduced as the Schiff base.

Prep. No.	Aminoketone	Melting point	Yield (%)	% N	
				found	calc.
I	$\text{p-C}_2\text{H}_5\text{-C}_6\text{H}_4\text{-NH-CH-C}_6\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_5$ $\beta\text{-(p-Ethylanilino)-}\beta\text{-phenylpropiofenone}$	131-132°	41	4.51, 4.62	4.25
II	$\text{p-C}_2\text{H}_5\text{-C}_6\text{H}_4\text{-NH-CH-C}_6\text{H}_4\text{-OCH}_3\text{-p}$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_5$ $\beta\text{-(p-Ethylanilino)-}\beta\text{-(p-methoxyphenyl)-}$ propiofenone	116-117	23	4.20, 4.15	3.90
III	$\text{p-C}_2\text{H}_5\text{-C}_6\text{H}_4\text{-NH-CH-C}_6\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_4\text{-OCH}_3\text{-p}$ $\text{p-Anisyl-}[\beta\text{-(p-ethylanilino)-}\beta\text{-phenylethyl}]$ ketone	140-141	30	3.93, 4.19	3.90
IV	$\text{p-C}_2\text{H}_5\text{-C}_6\text{H}_4\text{-NH-CH-C}_6\text{H}_4\text{-OCH}_3\text{-p}$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_4\text{-OCH}_3\text{-p}$ $\text{p-Anisyl-}[\beta\text{-(p-ethylanilino)-}\beta\text{-(p-methoxy-}$ $\text{phenyl)-ethyl}] \text{ ketone}$	119-121	26	3.87, 3.89	3.60
V	$\text{p-C}_2\text{H}_5\text{-C}_6\text{H}_4\text{-NH-CH-C}_6\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_4\text{-CH}_3\text{-p}$ $\text{p-Tolyl-}[\beta\text{-(p-ethylanilino)-}\beta\text{-phenylethyl}]$ ketone	127-128	42	4.33, 4.33	4.08
VI	$\text{p-C}_2\text{H}_5\text{-C}_6\text{H}_4\text{-NH-CH-C}_6\text{H}_4\text{-OCH}_3\text{-p}$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_4\text{-CH}_3\text{-p}$ $\text{p-Tolyl-}[\beta\text{-(p-ethylanilino)-}\beta\text{-(p-methoxy-}$ $\text{phenyl)-ethyl}] \text{ ketone}$	123-125	37	3.45, 3.45	3.75
VII	$(4)\text{-H}_7\text{C}_3\text{-C}_6\text{H}_3\text{-}[(2)\text{-CH}_3\text{]-NH-CH-C}_6\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_2\text{-CO-C}_6\text{H}_5$ $\beta\text{-(2-Methyl-4-isopropylanilino)-}\beta\text{-phenyl-}$ propiofenone	163-164	21	4.14, 4.43	3.92

As already mentioned in the literature [1-4], heating of β -arylamino ketones with concentrated hydrochloric acid leads to hydrolysis to the original primary amine and chalcone.

EXPERIMENTAL

p-Ethylaniline was synthesized from p-nitroethylbenzene, prepared by the method of Schultz [5]. p-Aminocymene was prepared by the literature methods [6,7].

β -Arylamino ketones. 1st variant of synthesis. To a solution of 0.01 mole of aromatic amine in 5 ml of alcohol (heated on a water bath) was added a solution of 0.01 mole of aromatic aldehyde in 5 ml of alcohol, after which the reaction mixture was heated on a water bath for 30 min. Thereupon (without separation of the resulting Schiff base), 0.5 g of the amine hydrochloride and 0.01 mole of fatty-aromatic ketone were added, and the mixture again heated on a water bath for 30-40 min. After cooling in a refrigerator, the reaction product was isolated, usually in crystalline form. The crystals were treated with ammonia solution and recrystallized from a mixture of alcohol and benzene.

2nd variant of synthesis. A mixture of 0.01 mole of primary amine, 0.01 mole of benzylidenacetophenone, 0.5 g of amine hydrochloride, and 10 ml of alcohol was heated in a sealed test tube on a water bath for 1 to 2 hr. The reaction products were worked up as above.

The products of both variants were identified by analysis and by the absence of a melting-point depression in a mixed test.

Hydrolysis of amino ketones (I-VII). The compound (0.1 g) was heated with concentrated hydrochloric acid (5 ml) with shaking for 10-30 min on a boiling-water bath. After cooling, the acid layer was run off, and the residual solid product dissolved in alcohol and crystallized from the latter.

Cleavage of (I) gave p-ethylaniline and a chalcone with m.p. 56°; cleavage of (VII) gave p-aminocymene and the same chalcone, as confirmed by a mixed melting test with the authentic chalcone.

SUMMARY

Studies were made of the catalytic condensation of p-ethylaniline and p-aminocymene with chalcone, and of Schiff bases (prepared from p-ethylaniline or p-aminocymene and aromatic aldehydes) with fatty-aromatic ketones. Seven new β -arylamino ketones were synthesized.

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* Original Russian pagination. See C.B. translation.

** Russian translation.

SYNTHESIS OF o-HYDROXYBENZENEPHOSPHONIC ACID AND SOME OF ITS DERIVATIVES*

A. M. Lukin and I. D. Kalinina

All-Union Scientific Research Institute of Chemical Reagents

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o-Hydroxybenzenephosphonic acid has not previously been prepared [2,3]. However, its synthesis appeared possible by various routes, some of which have already been investigated for preparation of the m- and p-isomers, namely:

1) From aminobenzenephosphonic acid by diazotization and replacement of the diazo group by the hydroxy group [4,5]. In the opinion of Kosolapoff and Bell [5], this is the only route of practical value;

2) By replacement of halogen by hydroxy group in the corresponding halobenzenephosphonic acid. However, attempts to prepare p-hydroxybenzenephosphonic acid by this route have been unsuccessful [5]; the only compounds that have been synthesized by this route are 3-nitro-4-hydroxybenzene and 3-hydroxy-4-nitrobenzenephosphonic acids [5-7];

3) By demethoxylation of methoxybenzenephosphonic acids. Only p-hydroxybenzenephosphonic acid has been obtained (in low yield) by this route. Attempts to prepare o-hydroxybenzenephosphonic acid by this route were unsuccessful [8], although its 4-nitro derivative was indeed synthesized - the sole compound containing an o-hydroxyphosphonic grouping [9];

4) By the method of Doak and Freedman [10], starting from the corresponding aminophenol. There is no mention in the literature, however, of the possibility of synthesis of m- and p-hydroxybenzenephosphonic acids by this method; only negative results are reported for the ortho-isomer in which we are interested [8].

Synthesis by the first method was impracticable, due to the complexity of preparation of the starting o-aminobenzenephosphonic acid (the next communication will be devoted to this problem). We therefore decided to attempt the preparation of the acid of interest to us from o-aminophenol and from o-bromobenzenephosphonic acid.

It should be noted that in the few instances when the preparation of hydroxybenzenephosphonic acids has succeeded, the reactions have always gone better with derivatives of these acids. Hence, for synthesis by the reaction of Doak and Freedman, the starting substance taken at first was not o-aminophenol, but 2-amino-4-chlorophenol. A series of experiments run with this aminophenol under the conditions of [10] convinced us of the necessity for some modifications in the procedure. The objective of the modifications was to minimize the formation of diarylphosphonic acids. It was thus found expedient to perform the reaction in presence of excess PCl_3 throughout the whole of the reaction period. The sequence of introduction of reactants was altered with this in view; diazonium borofluoride was added to the reaction mass containing phosphorus trichloride, and not conversely as in [10]. In addition, the quantity of phosphorus trichloride was increased by about 20%. As a result, it was possible without undue difficulty to isolate 2-hydroxy-5-chlorobenzenephosphonic acid in the form of an equimolar mixture of the monopotassium salt with the free acid.

The first attempts to prepare o-hydroxybenzenephosphonic acid, even by a modification of the method of [10], nevertheless ended in failure. The instability of the C-P bond and the voluminous resin formation prevented the isolation of the acid in question either as such, or in the form of the potassium or sodium salt. In their place, apart from resin, we obtained only phenol in admixture with phosphoric acid salts.

*Communication II in the series "Investigations of arylphosphonic acids." For I see [1].

Having been unsuccessful in attempts to isolate the acid, we decided to demonstrate its formation by another method. For this purpose, we exploited its ability to couple with diazo compounds. We carried out this reaction directly with the reaction mass obtained in the appropriate manner, and obtained a phosphorus-containing azo dye (with the diazo compound from p-nitroaniline) in a yield of 12%.

In later experiments we were able to separate the barium salt of the acid. This salt was formed directly in the initial ethyl acetate medium, thus giving the possibility of avoiding a whole series of treatments of the reaction mass, promoting rupture of the C-P bond. From the isolated salt was prepared an azo dye with p-nitroaniline.

We obtained considerably better results in the investigation of the synthesis of o-hydroxybenzenephosphonic acid by the second route. Hydrolysis of o-bromobenzenephosphonic acid was effected both with caustic alkali and ammonia, with addition in both cases of cuprous oxide as catalyst; the reaction goes with adequate speed even at 70-80°. o-Hydroxybenzenephosphonic acid could not be isolated in chemically pure form when an alkaline medium was used; in this case, its formation was demonstrated, as before, by synthesis of a phosphorus-containing azo dye by coupling of the separated product with the diazo compound from p-nitroaniline. When using an ammoniacal medium, however, the chemically pure o-hydroxybenzenephosphonic acid could be isolated in a yield of 40%.

Our results differ appreciably from those obtained in replacement of bromine by hydroxyl in p-bromobenzenephosphonic acid; in the latter case, the reaction could not be realized [5]. In our case, the lability of the bromine was undoubtedly influenced to a decisive extent by the presence of the phosphonic group in the ortho-position, in complete agreement with analogous cases of the influence of a nitro group in the ortho-position.

Also worthy of note is the fact that our chosen conditions of hydrolysis of bromobenzenephosphonic acid in an ammoniacal medium are very similar to those described for the synthesis of o-aminobenzenephosphonic acid [4]. However, we did not detect even traces of the latter compound.

In the pure form, o-hydroxybenzenephosphonic acid was found to be a very stable compound, although we observed evidence of hydrolysis of the C-P bond in the course of its synthesis. It has a sharp melting point, and couples well with active diazo compounds, unlike its chloro derivative.

EXPERIMENTAL*

Synthesis of 2-hydroxy-5-chlorobenzenephosphonic acid by the method of Doak and Freedman. To a solution of 48 g of 2-amino-4-chlorophenol in 154 ml of hydrofluoboric acid (d 1.22) was added 28 g of sodium nitrite with stirring over a period of 1 hr at a temperature of -5 to +5°. The precipitate was filtered after the lapse of 30-40 min, washed twice with water, three times with ether, and dried in the air. Yield 49 g. To a mixture of 250 ml of anhydrous ethyl acetate with 23 ml of PCl₅ was added portionwise a mixture of 48.6 g of diazonium borofluoride and 4 g of cuprous bromide. During the addition of the diazonium borofluoride, the temperature gradually rose to 45-50°, and nitrogen started to come off. After the diazonium compound had been added, the reaction mass was held at the same temperature until nitrogen ceased to come off (3-5 hr). Then the precipitate was filtered and 60 ml of distilled water was added dropwise to the filtrate at 20-30°. Thereupon, the ethyl acetate was distilled off with steam; the reaction mass was cooled, and copper sulfide brought down. The latter was filtered and the acid filtrate heated until the odor of hydrogen sulfide had disappeared completely. The resulting solution was neutralized at first with saturated KOH solution (to pH 2), and then with crystalline KHCO₃; completion of neutralization was checked with Congo Red paper (absence of a blue stain when a drop of the solution was placed on the paper). The mass was later evaporated on a water bath; at first the inorganic salts came down and were filtered; evaporation to a volume of 50 ml gave a crystalline precipitate of the salt of the synthesized acid. The salt was crystallized from water and alcohol. Yield 5.5 g (12.5%).

Found %: P 13.49, 13.49; Cl 15.81, 15.63; K 8.52. C₆H₅O₄PClK · C₆H₅O₄FCI. Calculated %: P 13.61; Cl 15.58; K 8.59.

*With participation of G. B. Zavarikhina and G. P. Stepanova. All determinations of P, Cl, and K contents in the compounds were carried out by the procedure described in [11].

Synthesis of o-hydroxybenzenephosphonic acid by the method of Doak and Freedman. To a solution of 30 g of o-aminophenol in 90 ml of hydrofluoboric acid (d 1.22) was gradually added 20.5 g of sodium nitrite in one hr with stirring, and at -8 to 0° . After 30-40 min, the precipitate was filtered, washed twice with iced water (40 ml), and three times with ether (50 ml), and dried in air to constant weight. Yield of diazonium borofluoride 42 g. To a mixture of 170 ml of anhydrous ethyl acetate with 23 ml of phosphorus trichloride was added, with intensive stirring at 35° , a mixture of 41.6 g of diazonium borofluoride and 4 g of cuprous bromide. During the addition the temperature rose to $45-50^{\circ}$, and nitrogen started to come off. After the whole of the diazonium salt had been added, the temperature was held at $45-50^{\circ}$ until no more nitrogen came off (3-5 hr). The precipitate was thereupon filtered and to the filtrate was added dropwise 60 ml of distilled water at $20-30^{\circ}$. The reaction mass was further worked up by two methods.

a) First method. Ethyl acetate was distilled with steam from the reaction mass after decomposition with water (distillation was continued until the cloudiness of the distillate disappeared). The reaction mass was then cooled, copper sulfide was precipitated, and the filtrate boiled with carbon until the H_2S was eliminated. It was then filtered. The mass was cooled and neutralized first with saturated KOH solution (until neutral to Congo), and then with $KHCO_3$ until weakly alkaline (test with Brilliant Yellow paper). To the resulting solution was added in small portions 15 g of p-nitroaniline diazonium borofluoride. Completion of coupling was marked by appearance in the reaction mass of a slight excess of diazonium compound that persisted for several minutes (test with H acid in sodium carbonate solution) when the medium was slightly alkaline. A dark-brown precipitate formed and was filtered, dissolved in 5% KOH solution, and again filtered. The filtrate was then acidified with hydrochloric acid until the reaction was acid (to Congo). The resulting precipitate was twice recrystallized from boiling water. Yield 8 g (12.5%).

Found %: P 8.16, 8.41; N 11.40, 11.36; K 10.44. $C_{12}H_9O_6N_3PK$. Calculated %: P 8.57; N 11.60; K 10.81.

b) Second method. To the reaction mixture obtained after decomposition with water was added (with vigorous stirring) 15.5 g of Na_2CO_3 ; the resulting precipitate was filtered; the copper in the filtrate was brought down with hydrogen sulfide, and the copper sulfide filtered off; the filtrate was neutralized with Na_2CO_3 to pH 2 to 3 (test with universal indicator paper). With progressive addition of Na_2CO_3 , two layers formed. The aqueous layer was separated and extracted with ethyl acetate to give a colorless extract. To the ethyl acetate solution was then added 63 g of $Ba(OH)_2 \cdot 8H_2O$. The precipitate was filtered; two layers again formed in the filtrate; the aqueous layer was separated, and the barium salt of o-hydroxybenzenephosphonic acid again extracted from it with ethyl acetate; the second extract was added to the main ethyl acetate mother liquor, and then the ethyl acetate was taken off in vacuo. To the syrupy mass remaining at the bottom of the flask was added 100 ml of alcohol. The precipitated barium salt was filtered off, washed by decantation with hot water until chloride ion had disappeared, filtered, pressed on filter paper, and dried at 120° . Yield 10 g of yellowish solid (16%).

Found %: Ba 43.3, 43.09; P 9.65, 9.69. $C_6H_5O_4PBa$. Calculated %: Ba 44.4; P 10.01.

A solution of 6.2 g of barium o-hydroxybenzenephosphonate in 150 ml of 5% Na_2CO_3 solution was prepared; the resulting precipitate was filtered off and into the filtrate was stirred a diazonium chloride solution prepared from 2.7 g of p-nitroaniline. The coupling reaction was checked in the manner described previously. After completion of the reaction, the mass was acidified with hydrochloric acid (test with Congo). The precipitate was filtered and the filtrate acidified with hydrochloric acid. This second precipitate was filtered, washed with cold water, and dried at 100° . Yield 1.5 g. Analysis showed the absence of sodium.

Found %: P 9.50, 9.57; N 12.88, 13.01. $C_{12}H_{10}O_6N_3P$. Calculated %: P 9.59; N 13.01.

Synthesis of o-hydroxybenzenephosphonic acid from o-bromobenzenephosphonic acid.* a) In 10% sodium hydroxide solution. To a solution of 12 g of o-bromobenzenephosphonic acid in 60 ml of 10% sodium hydroxide solution with stirring was added a slurry containing 9 g of freshly prepared cuprous oxide, and the mixture was heated at $70-80^{\circ}$ for 12 hr. The mass was then filtered and the filtrate acidified with hydrochloric acid to pH 4. The copper was brought down with hydrogen sulfide, the sulfide filtered off, the filtrate boiled with carbon and again filtered; the colorless filtrate was then evaporated on a water bath to about half its volume. The resulting

*o-Bromobenzenephosphonic acid was obtained under conditions similar to those described in [5,12], but modified in the way given in the general part.

precipitate of inorganic salts was filtered and evaporation of the filtrate was continued to a volume of 20-30 ml. The second precipitate was again filtered and dried at 100°. There was obtained 8.5 g of white crystals comprising a mixture of o-hydroxybenzenephosphonic acid and NaCl. This mixture could not be easily separated by crystallization. The coupling method was therefore used to demonstrate the presence of the acid. The precipitate was dissolved in 60 ml of 10% sodium carbonate solution, and a diazonium chloride solution (from 4 g of p-nitroaniline) was stirred in. Later steps in the synthesis of the dye were similar to those described in the previous experiment. Weight of dye after purification 2.7 g (16.3%). Analysis confirmed the absence of sodium.

Found %: P 9.43, 9.28; N 13.52, 13.43. $C_{12}H_{13}O_6N_3P$. Calculated %: P 9.59; N 13.01.

b) In an ammoniacal medium. To a solution of 23.7 g of o-bromobenzenephosphonic acid in 400 ml of ammonia solution (d 0.9) was added in three portions (in the course of an hour) 18 g of cuprous oxide in the form of a freshly prepared slurry. The reaction mass was stirred at 70° for 13 hr. The ammonia concentration in the mass was kept constant by passage of gaseous ammonia (for an hour) at intervals of 2 hours. The reaction mass was then cooled and acidified with concentrated hydrochloric acid to pH 3-4. A greenish precipitate came down and was filtered and dissolved in dilute hydrochloric acid (1:2). The copper was brought down with hydrogen sulfide, the sulfide was filtered off, and the mother liquor was boiled with carbon, filtered, and neutralized with sodium carbonate until a blue stain ceased to be formed from a drop of the solution on Congo paper. The white, crystalline precipitate was washed with water until free of chloride ion, and dried at 120°. Yield of acid 7.1 g (41%). Tests for sodium and for amine (by diazotization and coupling) were negative.

Found %: C 41.43, 41.31; H 4.56, 4.50; P 17.61, 17.67. $C_6H_7O_4P$. Calculated %: C 41.39; H 4.05; P 17.79.

The o-hydroxybenzenephosphonic acid was a white, crystalline substance with m.p. 178-179° (rate of heating 2.5-3° per min); it gave a characteristic orange-brown color with ferric chloride. Heating of 1 g of o-hydroxybenzenephosphonic acid with concentrated hydrochloric acid for 3 hr gave 0.3 g of a substance whose melting point was close to that of the chemically pure acid; a mixture with the latter did not exhibit an appreciable depression of melting point.

SUMMARY

o-Hydroxybenzenephosphonic acid and some of its derivatives were prepared for the first time. It was established that hydrolysis of o-bromobenzenephosphonic acid in ammonia solution is the simplest method of synthesis of o-hydroxybenzenephosphonic acid.

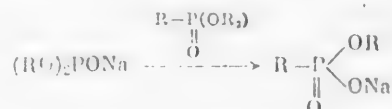
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*Original Russian pagination. See C.B. translation.

methylenediphosphonic, ethylphosphinic, and chloromethylphosphinic acids. The low-boiling fraction consists mainly of diethyl esters of ethyl- and chloromethylphosphinic acids.

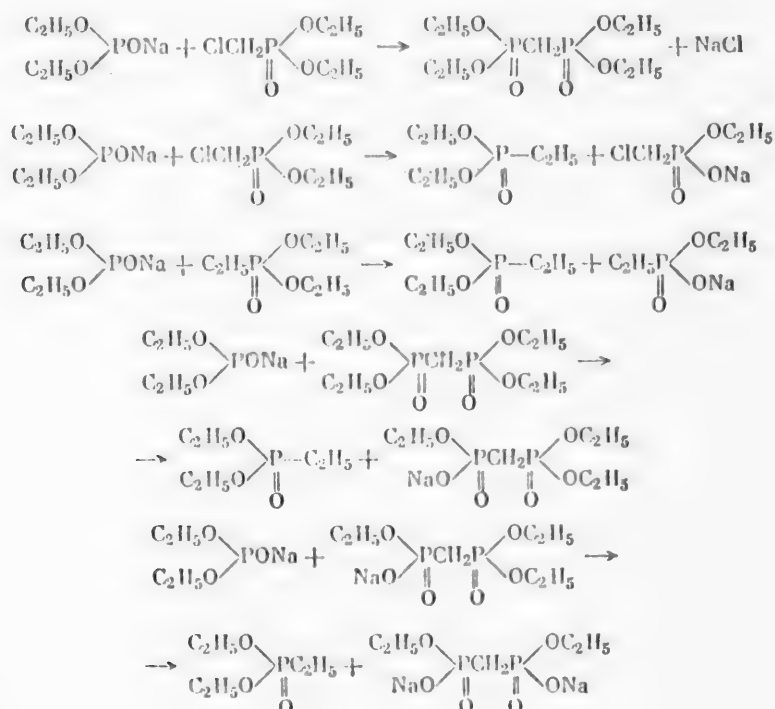
Formation of these products can be explained as the result of alkylation of sodium dialkyl phosphites by neutral esters of alkylphosphinic acids. We previously studied this reaction [5] and proposed it as a method of preparation of phosphonates. It was shown that heating of sodium dialkyl phosphites with a small addition of neutral alkyl phosphonates led to good yields of salts of esters of alkylphosphinic acids.



A similar result is obtained when sodium dialkyl phosphites are heated with catalytic quantities of alkyl halides.

In accord with these investigations, the formation of diverse products when esters of chloromethylphosphinic acid react with sodium dialkyl phosphites is the consequence of alkylation of the latter by the phosphonates formed. Participating in these reactions are neutral esters of methylenediphosphonic, chloromethylphosphinic, and ethylphosphinic acids. The ester of chloromethylphosphinic acid alkylates sodium dialkyl phosphite in its capacity as an alkyl halide and a phosphonate. We indirectly demonstrated the ability of this ester to alkylate sodium dialkyl phosphite at the expense of the ester group (see below). The ability of neutral diphosphonates to alkylate sodium dialkyl phosphites was proven in this investigation by direct experiment. Heating of equimolar quantities of sodium diethyl phosphite and tetraethyl methylenediphosphonate under conditions similar to those in the synthesis of the latter by the action of diethyl chloromethylphosphonate on sodium diethyl phosphite gave the diethyl ester of ethylphosphinic acid (yield 40%), a small quantity of the original diphosphonate, and a saltlike product containing the ester-salt of methylenediphosphonic acid.

Consequently, the formation of all the above products in the reaction of sodium diethyl phosphite with the diethyl ester of chloromethylphosphinic acid can be represented by the following scheme:

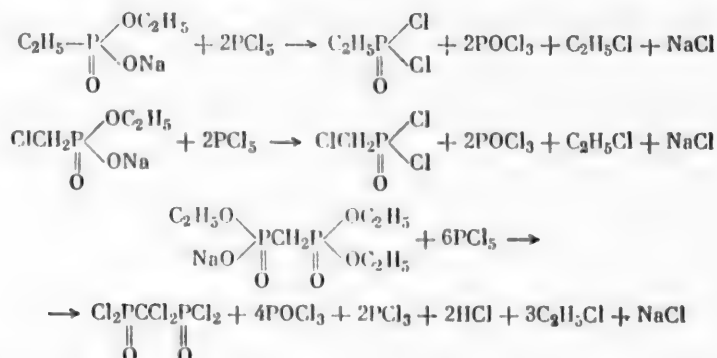


We carried out the reaction between sodium diethyl phosphite and the diethyl ester of chloromethylphosphinic acid under various conditions — use of different solvents (ether, benzene, toluene), various temperatures and durations of heating. The sequence of mixing of reactants was also varied.

Considerable difficulties are encountered in the separation of the substances formed in the reaction. The reaction mass was treated with ligroine for separation of the solid, saltlike products from the liquid phase,* after which the salt could be easily filtered. The dried solid consisted of sodium chloride (about 70% of the weight of the precipitate and 55% of the theoretical yield) and a mixture of salts of esters of ethylphosphinic, chloromethylphosphinic, and methylenediphosphonic acids.** The ester-salts were separated from the sodium chloride by solution in alcohol.

The filtrate, after distillation of the solvent, was subjected to fractional distillation in vacuo. In all cases a considerable quantity of low-boiling fraction was obtained (70–120° at 6–8 mm), which consisted mainly of two products — the diethyl ester of ethylphosphinic acid and the diethyl ester of chloromethylphosphinic acid. These compounds were obtained pure by numerous fractional distillations.*** The yield of diethyl phosphonate, depending on the experimental conditions, was 30–50% (on the sodium diethyl phosphite).

After the neutral ester of methylenediphosphonic acid had been distilled off, the flask always contained a considerable amount of glassy product which consisted of salts of esters of ethylphosphinic, chloromethylphosphinic, and methylenediphosphonic acids with a small admixture of sodium chloride. The presence of these substances in the residue obtained after distillation of the diphosphonate and in the solid products isolated from the reaction mass by treatment with ligroine was confirmed by transformation of the ester-salts into chlorides of the respective acids by the action of phosphorus pentachloride; in this way, the ester-salts of ethyl- and chloromethylphosphinic acids were converted, respectively, into the dichlorides of ethyl- and chloromethylphosphinic acids, while ether-salts of methylenediphosphonic acid were converted into tetrachlorides of dichloromethylenediphosphonic acid.



The first two acid chlorides could not be isolated in the pure form, due to the closeness of their boiling points. However, from the boiling point of the low-boiling fraction (70–80° at 10 mm), the specific gravity and the chlorine content, we have ample evidence that this fraction consists mainly of a mixture of the dichlorides of ethyl- and chloromethylphosphinic acids. The specific gravity of this fraction varied in different experiments, but always had a value intermediate between the specific gravities of the dichlorides of ethyl- and chloromethylphosphinic acids. The chlorine content, determined after hydrolysis, was slightly lower than the value calculated for the dichloride of ethylphosphinic acid. After mineralization, the chlorine content was found to have increased appreciably and occupied a position intermediate between the calculated content of chlorine in the dichlorides of ethyl- and chloromethylphosphinic acids. On the basis of the chlorine content found after hydrolysis and after

* In other experiments, aiming at separation only of the neutral esters of methylenediphosphonic acid, a small quantity of water was added to the reaction mass for precipitation of the saltlike products. The salts were washed out with water when water-insoluble diphosphonates were being prepared.

** The quantity of sodium chloride was determined by titration of the chloride ion (without mineralization of the substance). It should be noted that some investigators [6] regarded the precipitate formed on alkylation of sodium dialkyl phosphites with alkyl halides as the pure salt of the hydrogen halide.

*** Due to the impossibility of quantitative resolution of the mixture of these products (similarity in boiling points), the content of ester of chloromethylphosphinic acid was calculated from the quantity of chlorine, determined after mineralization of the mixture of substances.

TABLE 1

Formula	Boiling point (pressure in mm)	n_D^{25}	n_D^{30}	M_R	
				calc.	found
(iso-C ₄ H ₉ O) ₂ P(O)CH ₂ Cl	72-73° (2)	1.0170	1.4333	50.26	50.30
(n-C ₄ H ₉ O) ₂ P(O)CH ₂ Cl	110-111° (2)	1.0786	1.4430	59.49	59.69
(n-C ₄ H ₉ O) ₂ P(O)CH ₂ P(O)(OC ₄ H ₉) ₂	193-194° (2)	1.0440	1.4426	102.44	101.86
(C ₂ H ₅ O) ₂ P(O)CH ₂ P(O)(OC ₄ H ₉) ₂	179-180° (2)	1.0943	1.4414	83.96	83.34
Cl ₂ P(O)CCl ₂ P(O)Cl ₂	139-140° (7)	—	—	—	—
M.p. 75-76°					

mineralization, the quantitative ratio of these two chlorides in the mixture was roughly estimated. The data confirm that the original mixture of salts contained salts of esters of ethyl- and chloromethylphosphinic acids. The presence of the latter ester-salt was confirmed and its approximate quantity determined also from the chlorine content found after mineralization of a weighed sample of the mixture of salts which had been thoroughly freed of sodium chloride by treatment with alcohol.

The tetrachloride of dichloromethylenediphosphonic acid was isolated and characterized. We also obtained this acid chloride in good yield by treating tetraethyl methylenediphosphonate with phosphorus pentachloride.

In the light of the foregoing facts, we can assume that the main cause of the low yields of methylenediphosphonates obtained by the Michaelis-Becker method is the alkylation of sodium dialkyl phosphites by neutral phosphonates and diphosphonates with formation of salts of esters of alkylphosphinic and diphosphonic acids. These secondary reactions are not limited to the preparation of methylenediphosphonates; they also take place during synthesis of esters of alkylphosphinic acids by the Michaelis-Becker method. In some cases, these secondary processes can be suppressed by suitable choice of conditions, but it hardly seems possible that they can be completely eliminated.

By reaction of esters of chloromethylphosphinic acid with sodium dialkyl phosphites we obtained the previously undescribed tetrabutyl and diethyldibutyl esters of methylenediphosphonic acid. Attempts to prepare the tetramethyl ester by this route were unsuccessful. This failure is apparently due to the high alkylating activity of methyl esters of chloromethyl- and methylphosphinic and methylenediphosphonic acids toward sodium dimethyl phosphite.

Esters of chloromethylphosphinic acid, needed for the synthesis of methylenediphosphonates, were obtained by the action of the dichlorides on alcohols; for this purpose we devised a modified procedure. The modification involved removal of the hydrogen chloride formed in the reaction in the course of addition of the acid chloride to the alcohol, by passage of a stream of dry air through the reaction mixture. The reaction mass was fractionated immediately after elimination of the hydrogen chloride without standing overnight as was the earlier practice [7]. In this way, it was possible to increase the yield of esters to 90-95% (previously 55-75% by other workers [7]). By this method we obtained the previously undescribed diisopropyl and dibutyl esters of chloromethylphosphinic acid. The properties of the compounds are set forth in Table 1.

EXPERIMENTAL

Reaction of sodium diethyl phosphite with diethyl ester of chloromethylphosphinic acid. Dropwise addition was made, with stirring, of 52.2 g of the diethyl ester of chloromethylphosphinic acid to a solution of the sodium salt of diethyl phosphite, prepared from 38.6 g of diethyl phosphite and 6.45 g of metallic sodium, in 100 ml of dry benzene. The reaction mass was heated on a water bath until trivalent phosphorus was absent (test with mercuric chloride). This step required about 6 hr. After cooling of the mixture, 50 ml of ligroine was added. On the following day the precipitate was filtered off, washed with ligroine, and dried. There was obtained 12.1 g of solid product containing 8.7 g (53%) of sodium chloride. The latter was determined by titration of the ionic chlorine.

Found %: Cl 43.5. NaCl. Calculated %: Cl 60.7.

The product also contained 3.4 g of the sodium salts of the ethyl esters of methylenediphosphonic, chloromethylphosphinic, and ethylphosphinic acids. The ester-salts were purified from sodium chloride by dissolution in anhydrous alcohol, and their content of phosphorus and chlorine was determined (found %: P 19.21, Cl 4.95).

The ester-salts were converted to acid chlorides by the action of phosphorus pentachloride, as detailed below. Fractional distillation of the filtrate gave two fractions: 1st, 70-120° (6 mm), 30 g; 2nd, 166-170° (6 mm, 45 g). The residue in the flask (a vitreous mass) weighed 10 g.

The first fraction contained about 10.7 g of the original ester of chloromethylphosphinic acid; this was determined from the chlorine content after mineralization of the substance (found % Cl 6.7). It also contained about 19.3 g (41.5% based on the sodium diethyl phosphite) of diethyl ester of ethylphosphinic acid. Numerous fractionations enabled the isolation of esters of chloromethyl- and ethylphosphinic acids in pure form. The first substance had b.p. 109-110° (10 mm), d_{20}^{20} 1.997, n_D^{20} 1.4424; the second had b.p. 84-86° (10 mm), d_{20}^{20} 1.0253, n_D^{20} 1.4162.

Redistillation of the second fraction gave 44.5 g (55% on the ester of chloromethylphosphinic acid taken and 69.5% on the ester entering into reaction) of tetraethyl ester of methylenediphosphonic acid; b.p. 152-153° (4 mm).

The residue remaining in the flask after distillation of the filtrate was freed of sodium chloride by dissolution in anhydrous alcohol. It was then analyzed for phosphorus and chlorine (found % P 19.56, Cl 5.20) and treated with phosphorus pentachloride. An energetic reaction occurred and ethyl chloride was evolved. The mixture was then held at 120-150° until phosphorus oxychloride ceased to be evolved. The residue in the flask was diluted with dry carbon tetrachloride and, with the objective of decomposition of the residual phosphorus pentachloride, dry sulfur dioxide was passed into the suspension until no further heat was generated. The sodium chloride was filtered; solvent, thionyl chloride, and phosphorus oxychloride were distilled off from the filtrate, and the residue was fractionated in vacuo. Two fractions were obtained: 1st, 70-80° (10 mm), 3.5 g; 2nd, 140 to 148° (10 mm), 3.2 g. The first fraction had d_{20}^{20} 1.4950 and contained 46.3% of chlorine (after hydrolysis with alkali) and 55.4% of chlorine after mineralization. Redistillation of the second fraction gave the tetrachloride of dichloromethylenediphosphoric acid with b.p. 139-140° (7 mm). The chloride crystallized from diethyl ether as well-formed, large crystals; m.p. 75-76°.

Found %: Cl (after mineralization) 66.48; Cl (after hydrolysis) 44.81; P 19.29, 19.20. $\text{CO}_2\text{P}_2\text{Cl}_6$. Calculated %: Cl (total) 66.75; Cl (as acid chloride) 44.50; P 19.44.

Dichloromethylenediphosphinyl tetrachloride. To 0.6 mole of phosphorus pentachloride was added 0.1 mole of tetraethyl methylenediphosphonate in small portions from a dropping funnel with shaking. After the violent reaction had subsided, the mixture was held at 120-140° until phosphorus oxychloride ceased to distil over. The residual phosphorus pentachloride was decomposed with sulfur dioxide. Distillation gave 22.9 g of the acid chloride (72%); b.p. 139-140° (7 mm); m.p. 75-76°.

Alkylation of sodium diethyl phosphite with tetraethyl methylenediphosphonate. A mixture of 0.1 mole of tetraethyl methylenediphosphonate and 0.1 mole of sodium diethyl phosphite in 50 ml of dry benzene was heated on a boiling bath for 6 hr. The solvent was distilled off from the reaction mass, after which the flask, through a trap immersed in a mixture of acetone and carbon dioxide, was connected to a vacuum of 1-2 mm, carefully heated to 100°, and held at this temperature for 1 hr. Distillation of the condensate yielded 6.6 g (40%) of diethyl ester of ethylphosphinic acid with b.p. 84-85° (13 mm), d_{20}^{20} 1.0257, n_D^{20} 1.4162. The residue in the flask was a glassy mass and consisted mainly of the sodium salt of the ester of methylenediphosphonic acid. Due to the difficulty of isolation in the pure state, this salt was not examined more closely.

Tetraethyl ester of methylenediphosphonic acid. To 0.1 mole of sodium dibutyl phosphite, prepared from 19.4 g of dibutylphosphorous acid and 2.3 g of metallic sodium in 50 ml of dry toluene, was added, with stirring, 0.1 mole of dibutyl ester of chloromethylphosphinic acid. The reaction mass was heated on a boiling water bath until trivalent phosphorus was absent (about 6 hr). Water was added to the cooled mixture until the saltlike products had dissolved. The aqueous layer was separated, and the organic layer was washed with water and dried over calcined potassium carbonate. After the solvent had been distilled off, the residue was fractionated in vacuo to give 20 g (50%) of product; b.p. 193-194° (2 mm).

Found %: P 15.25, 15.40. $\text{C}_{17}\text{H}_{38}\text{O}_6\text{P}_2$. Calculated %: P 15.47.

Diethyldibutyl ester of methylenediphosphonic acid. From 0.1 mole of sodium diethyl phosphite and 0.1 mole of dibutyl ester of chloromethylphosphinic acid (conditions similar to those for synthesis of tetraethyl methylene diphosphonate) was obtained, after two distillations, 15.5 g (45%); b.p. 179-180° (2 mm).

TABLE 2

Formula	Yield (%)	Found (%)		Calc. (%)	
		P	Cl	P	Cl
(iso-C ₃ H ₇ O) ₂ P(O)CH ₂ Cl	79	14.50	16.57	14.43	16.52
(n-C ₄ H ₉ O) ₂ P(O)CH ₂ Cl	94	12.70	14.58	12.77	14.61
(C ₂ H ₅ O) ₂ P(O)CH ₂ Cl	90	Previously obtained, yield 55% [7]			
(C ₂ H ₅ O) ₂ P(O)CH ₂ Cl	91.5	Previously obtained, yield 75% [7]			

Found %: C 44.79, 44.92; H 8.91, 8.69; P 17.99, 18.11. C₁₅H₃₅O₆P₂. Calculated %: C 45.34; H 8.78; P 17.99.

Esters of chloromethylphosphinic acid. To 1.3 moles of anhydrous alcohol was added 0.5 mole of chloromethylphosphinyl chloride dropwise in the course of 40-50 min while the mass was cooled with ice and salt, and a powerful stream of dry air was passed through. Aspiration of air was continued until the whole of the hydrogen chloride had been removed from the reaction mass (3-4 hr). The residue was then distilled in vacuo. Yield and analytical data are set forth in Table 2.

SUMMARY

The reaction of sodium dialkyl phosphites with esters of chloromethylphosphinic acid was studied. It was shown that neutral esters of methylenediphosphonic, chloromethylphosphinic, and alkylphosphinic acids alkylate sodium dialkyl phosphites with formation of salts of esters of these acids. These alkylation reactions are a principal cause of the low yields of phosphonates and diphosphonates in the Michaelis-Becker reaction.

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DIPHOSPHONATES

II. SYNTHESIS OF ESTERS OF ETHYLENE- AND METHYLETHYLENEDIPHOSPHONIC ACIDS

K. A. Petrov, F. L. Maklyaev, and N. K. Bliznyuk

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Ethylenediphosphonates, like methylenediphosphonates, have been little studied. Several ethylenediphosphonates have been described, and the first representative — the tetraethyl ester — was obtained as recently as 1947. These compounds were prepared by two routes: by alkylation of neutral phosphites with ethylene bromide [1,9], and by addition of dialkyl phosphites to esters of vinylphosphinic acid [2]. Attempts to prepare ethylenediphosphonates by reaction of sodium salts of dialkylphosphorous acids with 1,2-dihaloalkanes, particularly dichloro- and dibromoethane, were unsuccessful [3]. Formation of a certain quantity of diphosphonate by the action of dibromoethane on sodium phosphite has also been reported [4].

The authors in question do not give the yields of the products formed.

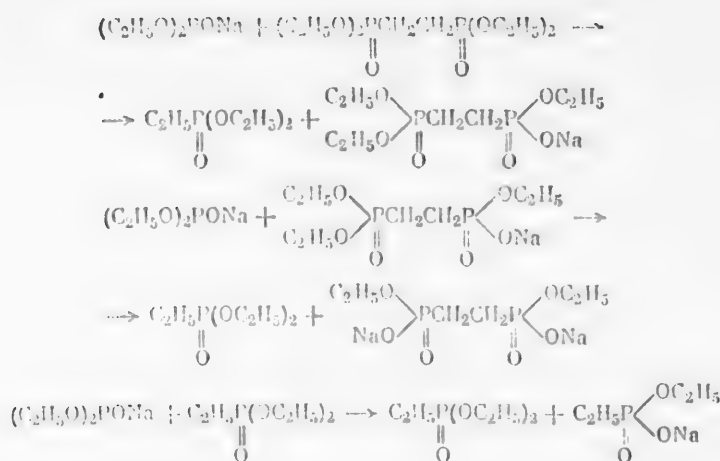
Our investigations have shown that the conditions for the above experiments could not result in formation of appreciable quantities of diphosphonate.

In the present work, it was shown that esters of ethylenediphosphonic acid can be synthesized by the Michaelis-Becker reaction. We succeeded in eliminating all the difficulties associated with the application of this method by determination of two parameters — firstly the optimum working temperature of the reaction and, secondly, the best sequence of mixing of reactants. It was found that in the reaction of sodium dialkyl phosphites with 1,2-dihaloalkanes, the olefines come off at only slightly raised temperature (about 30° for dibromoethane and 60° for dichloroethane when starting from sodium diethyl phosphite). In the cases of sodium diisopropyl phosphite and sodium dibutyl phosphite, the olefin separates at higher temperature. Mainly diphosphonate is formed at the temperatures given below.

The sequence of mixing of reactants also has a marked influence on the direction of the reaction. The yield of diphosphonate does not exceed 42% if dichloroethane is added to a benzene solution of sodium diethyl phosphite and the mixture is heated at 50-55°. In this case, the diethyl ester of ethylphosphinic acid and salt-like products are formed in considerable quantity (the saltlike products are salts of esters of ethylenediphosphonic and ethylphosphinic acids). On the other hand, the yield of diphosphonate increases to 57.5% if the benzene solution of the sodium salt is slowly added to dichloroethane previously heated to 50-55°, and the formation of ester of ethylphosphinic acid and of saltlike products is correspondingly reduced.

Esters of halodiethylphosphinic acid are not detected when sodium diethyl phosphite is added to dichloro- and dibromoethane in any excess. This is evidently due to the greater mobility of the halogen in the ester of β -haloethylphosphinic acid in comparison to that in 1,2-dihaloalkanes. We experimentally confirmed the high mobility of halogen in esters of β -haloethylphosphinic acid in a study of the reaction of sodium diethyl phosphite with the diethyl ester of β -bromoethylphosphinic acid. This reaction takes place under very mild conditions, and leads to diphosphonate in good yield. In this connection, doubts arise as to the correctness of the data of other investigators [4] for the preparation of the ester-salt of β -bromoethylphosphinic acid by the reaction of sodium diethyl phosphite with dibromoethane.

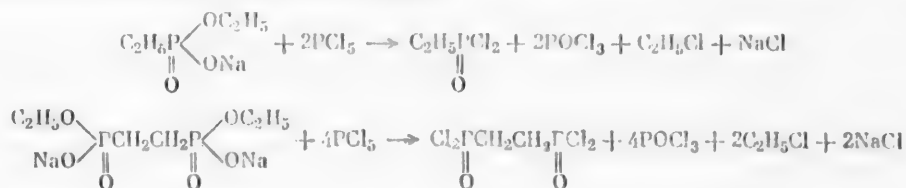
Formation in this reaction of a neutral ester of ethylphosphinic acid, together with ester salts of ethylphosphinic and ethylenediphosphonic acids, is accounted for by alkylation of sodium diethyl phosphite by the tetraethyl ethylenediphosphonate and the diethyl ethylphosphonate formed in the reaction.



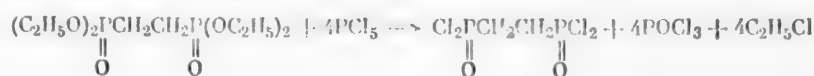
These reactions are similar to those that we studied in connection with alkylation of sodium dialkyl phosphites, with small additions of neutral esters of alkylphosphinic acids [5], and with the synthesis of methylenediphosphonates [6]. With the objective of confirming the alkylating ability of tetraethyl ethylenediphosphonate, the latter was heated with sodium diethyl phosphite. From the reaction mass was isolated the ester of ethylphosphinic acid (40% yield), and this was converted to the dichloride (yield 80%) for the purpose of identification.

The cause of the increased yield of neutral ester of ethylenediphosphonic acid when the usual sequence or mixing of reactants is reversed can be understood if allowance is made for the above-noted alkylation of sodium dialkyl phosphite by neutral esters of alkylphosphinic and diphosphonic acids. There will obviously be an excess of alkyl halide if sodium dialkyl phosphite is slowly added to a heated alkyl halide, and this will, of course, ensure formation of neutral ester and create unfavorable conditions for secondary reactions of alkylation of sodium phosphite by the diphosphonates and phosphonates formed.

The presence in the saltlike residue, after distillation of the diphosphonate, of ester-salts of ethylenediphosphonic and ethylphosphinic acids was demonstrated by treatment of this residue with phosphorus pentachloride. This treatment converted the ester-salts into the corresponding chlorides of ethylphosphinic and ethylenediphosphonic acids, which were isolated and characterized.



The second acid chloride was identical with the one easily obtainable by the action of phosphorus pentachloride on tetraethyl ethylenediphosphonate.



Alkylation of sodium dialkyl phosphites by dichloroethane was a route, not only to the tetraethyl ester, but also to the tetraisopropyl and tetrabutyl esters of ethylenediphosphonic acid. The tetraisopropyl ester has not previously been described. Esters of alkylphosphinic acids were also isolated from the products of reaction. This fact again demonstrates the high alkylating activity of diphosphonates.

The tetraethyl ester of ethylenediphosphonic acid was also obtained by alkylation of sodium diethyl phosphite by the ester of β -bromoethylphosphinic acid. It should be noted that, in this case, the formation of diphosphonate possibly does not proceed by the Michaelis-Becker mechanism. It might be assumed that, under

the influence of alkaline reagents under the reaction conditions, the β -bromoethylphosphonate is converted into an ester of vinylphosphinic acid,* which then adds on the dialkyl phosphite. This reaction also possibly takes place during alkylation of sodium dialkyl phosphites by 1,2-dihaloalkanes.

Esters of methylethylenediphosphonic acid were prepared by addition of dialkyl phosphites to allylphosphonates in presence of sodium alkoxides. This reaction has already been studied [8] and the previous authors reported that reaction of dialkyl phosphites with allylphosphonates in presence of alkoxides goes very slowly at 90-100°, and is considerably speeded up at 130-140°. We established that the rate of this reaction depends not so much on the temperature as on the quantity of catalyst added. With small quantities of alkoxide, the reaction does not go to completion even after prolonged heating of the reaction mixture in sealed tubes at 130-140°. With larger amounts of catalyst the reaction is completed in a short time, and the diphosphonate is obtained in a yield of over 80% (as against the 51.6% obtained by the earlier workers [8]).

Esters of allylphosphinic acid were obtained by reaction of allyl bromide with sodium dialkyl phosphites. This reaction has likewise been studied previously [8]. By changing the sequence of mixing of reactants, and altering the thermal conditions, we succeeded in raising the yield from 57 to 72.5%.

EXPERIMENTAL

Tetraethyl ethylenediphosphonate. a) To 31.5 g of dry dichloroethane (heated to 55°) was added dropwise, with stirring and heating, in the course of 3 hr, a freshly prepared hot solution of 67.3 g of sodium diethyl phosphite in 180 ml of dry benzene. After addition of the salt solution, the reaction mass was stirred at 50-55° for 6 hr. To the mixture was then added 5 ml of water. The resulting precipitate was filtered off, the filtrate dried over magnesium sulfate, the solvent distilled off, and the residue fractionated in vacuo. Two distillations gave 6.2 g of the diethyl ester of ethylphosphonic acid with b.p. 83-84° (9 mm), d^{20}_4 1.4160, and 36.9 g (59%) of tetraethyl ethylenediphosphonate with b.p. 164-165° (1 mm), d^{20}_4 1.4438.

b) To the sodium salt of diethylphosphorous acid, prepared from 3.2 g of sodium and 20 g of diethyl phosphite in 40 ml of dry ether, was added dropwise (with stirring and iced-water cooling) 34 g of the diethyl ester of β -bromoethylphosphinic acid in the course of 30 min. Sodium bromide came down at once. The mixture was stirred for 1 hr at 18-20°. The precipitate was filtered after addition of a few drops of water and brief stirring. Distillation of the filtrate gave 28 g (67%) of tetraethyl ethylenediphosphonate with boiling point and refractive index identical with those of the diphosphonate obtained from dichloroethane and sodium diethyl phosphite.

c) Starting components were 20.4 g of dibromoethane and 16.5 g of sodium diethylphosphite in 45 ml of dry benzene. Experimental conditions were the same as in a, except that the addition of sodium diethyl phosphite to dibromoethane was performed at such a speed that the temperature of the mixture did not rise above 30°, and the reaction mass after mixing of the reactants was stirred for an hour at 25-30°. Yield of tetraethyl ethylenediphosphonate 2.5 g (16.4%) with the same constants.

d) To sodium diethyl phosphite, prepared from 45.2 g of diethyl phosphite and 9.2 g of metallic sodium (wire), in 150 ml of benzene was added 19.8 g of dichloroethane dropwise with stirring. The reaction mass was heated at 50-55° for 8 hr, after which 100 ml of ligroine was added, and the mixture stood overnight. The next day the precipitate was filtered off, the solvent distilled off from the filtrate, and the residue fractionated in vacuo. There was obtained 12.3 g of the diethyl ester of ethylphosphinic acid, 16.1 g (40%) of tetraethyl ethylenediphosphonate, and 10.4 g of a saltlike undistillable residue which was freed of sodium chloride by dissolution in absolute alcohol. The saltlike product was treated with phosphorus pentachloride for the purpose of identification.

To a suspension of 10 g of the dry salt in 10 ml of phosphorus oxychloride was added 28 g of phosphorus pentachloride dropwise with shaking. An exothermic reaction took place and ethyl chloride was evolved. The reaction mass was heated to 100°; it was then heated in a sealed tube for 3 hr at 120-130°. A stream of dry sulfur

* The diethyl ester of vinylphosphinic acid was obtained by M. I. Kabachnik [7] by heating an ester of β -chloroethylphosphinic acid with alcoholic alkali. He recovered part of the original ester of β -chloroethylphosphinic acid unchanged. We repeated these experiments and established that the substance isolated from the reaction mixture, and assumed by Kabachnik to be the original substance, is the diethyl ester of ethoxyethylphosphonic acid. This product could be formed by addition of alcohol to vinylphosphonate.

dioxide was passed through the mass for decomposition of the excess of phosphorus pentachloride (until heat was no longer liberated). The sodium chloride was removed from the heated solution by filtration. Thionyl chloride and phosphorus oxychloride were distilled off from the filtrate. The flask was then connected to a vacuum through a condenser-trap cooled with a mixture of ice and salt, and heated to 100-120°. Ethylphosphinyl dichloride was isolated from the condensate by fractionation.

B.p. 71-72° (12 mm), d_4^{20} 1.3749, n_D^{20} 1.4641.

Found %: Cl 47.9, 48.1. $C_2H_5OPCl_2$. Calculated %: Cl 48.2.

After the distillation of the ethylphosphinyl chloride, the residue in the flask was a solid substance which easily dissolved in phosphorus oxychloride on heating. Recrystallization from phosphorus oxychloride, numerous washings with dry ether, and drying in vacuo gave the tetrachloride of ethylenediphosphonic acid as a white powder with m.p. 155-157° (decomp.).

Found %: P 23.32, 23.40; Cl 53.61, 53.68. $C_2H_4O_2P_2Cl_4$. Calculated %: P 23.43; Cl 53.80.

The chloride was poorly soluble in common organic solvents and, therefore, the best solvent for recrystallization was phosphorus oxychloride.

Alkylation of sodium diethyl phosphite by tetracthyl ethylenediphosphonate. A mixture of 0.1 mole of sodium diethyl phosphite and 0.1 mole of tetracthyl ethylenediphosphonate in 30 ml of benzene was heated at 70-80° for 8 hr. After the solvent had been distilled off, the flask was connected to a vacuum (1-2 mm) via a condenser-trap cooled with a mixture of ice and salt, and heated for 30 min on a boiling bath. Fractionation of the condensate gave 6.65 g (40%) of the diethyl ester of ethylphosphinic acid; b.p. 85-86° (12 mm). Treatment of this ester with phosphorus pentachloride gave ethylphosphinyl dichloride (80% yield), which was identified from its boiling point, specific gravity, refractive index, and chlorine content.

The residue in the flask was a vitreous mass containing the ester-salt of ethylenediphosphonic acid. The latter could not, however, be isolated in the pure form.

Tetraisopropyl ethylenediphosphonate. To a solution of 16.6 g of dichloroethane in 20 ml of benzene, heated to 70-80°, was slowly added a freshly prepared benzene solution of sodium diisopropyl phosphite, prepared from 7.7 g of sodium wire and 55.6 g of diisopropylphosphorous acid in 150 ml of benzene. For completion of the reaction the mixture was heated at the same temperature for 5 hr. Water was then added to the reaction mass (with cooling) until the precipitate dissolved. The benzene layer was separated, washed with 5% sodium carbonate solution and then with water, and dried over calcined magnesium sulfate. After the solvent had been distilled off, the residue was fractionated in vacuo. Two fractions were collected: 1st, 60-64° (1 mm), 9 g; 2nd, 140 to 150° (0.4-0.5 mm), 32 g. The first fraction consisted mainly of the diisopropyl ester of isopropylphosphinic acid. Redistillation of the second fraction gave 28 g (46.7%) of tetraisopropyl ethylenediphosphonate.

B.p. 144-145° (0.4 mm), d_4^{20} 1.0453, n_D^{20} 1.4320, M_R 88.94; calc. 88.59.

Found %: P 17.45, 17.40. $C_{14}H_{32}O_6P_2$. Calculated %: P 17.30.

The ester is easily soluble in organic solvents and poorly soluble in water.

Tetrabutyl ethylenediphosphonate. From 11.5 g of metallic sodium, 97 g of dibutyl phosphite, and 25 g of dichloroethane, under similar conditions to those in the synthesis of tetraisopropyl ethylenediphosphonate, was obtained 42.5 g (41%); b.p. 202-204° (3 mm); d_4^{20} 1.0238, n_D^{20} 1.4403. The ester was identical with the substance previously obtained in insignificant yield by reaction of tributyl phosphite with dibromoethane [9].

Tetracthylmethyl ethylenediphosphonate. a) To a mixture of 16.2 g of diethyl ester of allylphosphinic acid and 12.5 g of diethyl phosphite was added (dropwise with shaking) a saturated alcoholic solution of sodium ethoxide until heat ceased to be liberated (about 3 ml of catalyst was added in all). After heating on a boiling water bath for 30 min, the reaction mass was distilled in vacuo to give 23.2 g (8.5%); b.p. 164-165° (3 mm).

b) A mixture of 15 g of diethyl allylphosphonate, 11.7 g of diethyl phosphite, and 1 ml of saturated alcoholic sodium alkoxide solution was heated in a sealed tube for 4 hr at 130-140°. Two fractions were collected on distillation: 1st, 60-95° (2 mm), 20 g; 2nd, 163-166° (2 mm), 4 g. The second fraction consisted mainly of diphosphonate, while the second was a mixture of starting reactants. To this mixture was added 2.5 ml of

saturated alcoholic sodium alkoxide solution; considerable heat was liberated. Distillation gave 14 g of tetraethyl ester of methylethylenediphosphonic acid with b.p. 164-165° (3 mm).

Diethyl allylphosphonate. To a solution of 27.6 g of allyl bromide in 50 ml of dry benzene was added, with stirring, a freshly prepared solution of 35.8 g of sodium diethyl phosphite in 100 ml of benzene at such a rate that the temperature of the reaction mass did not rise above 25°. For completion of the reaction, the mixture was stirred for 30 min at 18-20°; this was followed by addition of a few milliliters of water. A dense layer of salt separated and was filtered off. The filtrate was dried over calcined magnesium sulfate and distilled in vacuo. Two fractions were collected: 1st, 77-80° (2 mm), 30.5 g; 2nd, 158-160° (2 mm), 3 g. Redistillation of the first fraction gave 29 g (73%) of diethyl ester of allylphosphonic acid with b.p. 78-79° (2 mm), d_{20}^{20} 1.0356, n_D^{20} 1.4350. The second fraction consisted mainly of the tetraethyl ester of methylenediphosphonic acid.

SUMMARY

1. A method was developed for preparation of ethylenediphosphonates involving reaction of sodium dialkyl phosphites with dichloroethane.
2. The method of preparation of esters of allylphosphonic and methylethylenediphosphonic acids was improved.

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SYNTHESIS OF 5-BROMOQUINOLINE

J. Bankovskis, L. A. Fedotova, and D. Ē. Zaruma

Institute of Chemistry, Academy of Sciences of the LatvSSR

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5-Halogenated quinolines, in particular 5-bromoquinoline, are usually obtained by the Skraup method. In spite of the simplicity of this general method of preparation of quinoline derivatives and the good yields of products, considerable difficulties arise in some cases in the isolation of the products from the reaction mixture, and in the separation of isomers. Due to the large volumes of reaction liquids in Skraup's synthesis of 5-bromoquinoline, which involves a series of steps, prolonged distillation with steam is necessary, and this must be followed by ether extraction of the 5-bromoquinoline from the large volume of distillate. The 5- and 7-isomers are formed in approximately equal quantities and must be separated. Their separation by the literature method [1] is very

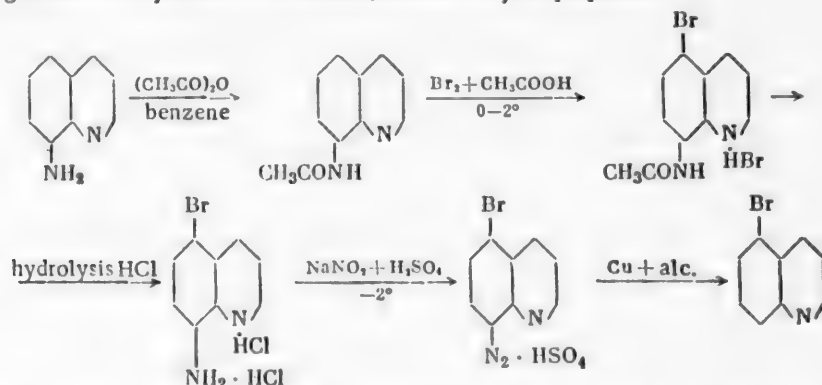
*Original Russian pagination. See C.B. translation.

rough. Even after two repetitions of the operation, the 5-bromoquinoline is contaminated with 7-bromoquinoline. Losses of 5-bromoquinoline are considerable: Part of the product remains in the mother liquor, and part is mixed with the 7-bromoquinoline. The net result is that the yield of pure 5-bromoquinoline does not exceed 10-20%, calculated on the *m*-bromoaniline.

Some investigators prefer to prepare 5-bromoquinoline by diazotization of 5-aminoquinoline, followed by replacement of the diazo group by bromine [2]. 5-Aminoquinoline is not a readily available substance; it can be prepared by reduction of 5-nitroquinoline, which in turn is obtained by nitration of quinoline (in admixture with 8-nitroquinoline, from which it must be separated) [3,4]. The two nitroquinolines are separated from one another by crystallization from dilute nitric acid. In the present case, the separation of the isomers is fairly satisfactory, but the subsequent reduction of 5-nitroquinoline to 5-aminoquinoline, in spite of its apparent fundamental simplicity, is unsatisfactory. Reduction of 5-nitroquinoline has been effected with stannous chloride in 50% yield or with iron in presence of acetic acid [4]. Our own numerous experiments on reduction of 5-nitroquinoline under various conditions were always accompanied by considerable resinification, and the yields of 5-aminoquinoline did not exceed 15-20%. The step of replacement of the amino group by bromine in 5-aminoquinoline has also given variable results, with yields of 5-bromoquinoline of between 15 and 60%.

We made an attempt to develop a method of preparation of 5-bromoquinoline from 8-aminoquinoline. The latter has become readily accessible on the basis of the method of N. N. Vorozhtsov and I. M. Kogan [6] for amination of 8-hydroxyquinoline with ammonia in presence of ammonium bisulfite. G. I. Mikhailov [7] improved this method, and raised the yield of 8-aminoquinoline to 81-83%. Hurdis [8] raised the yield of 8-aminoquinoline to 93%. Our experiments on the preparation of 8-aminoquinoline by Mikhailov's modification gave results in general agreement with this author.

The following scheme for synthesis of 5-bromoquinoline may be proposed:



Claus and Setzer found that bromination of 8-aminoquinoline in the cold in a medium of acetic acid or chloroform leads to 5,7-dibromo-8-aminoquinoline [9]. The same authors found that a monobromo derivative can be obtained by bromination of 8-acetylaminoquinoline. In this case, the bromine is exclusively in the 5-position. Acetylation of 8-aminoquinoline is effected with acetic anhydride in a medium of acetic acid. Acetylation in benzene gives the best results. The product is obtained in good yield, with m.p. 104° (the literature [10] gives 103°), but does not crystallize completely from the mother liquor. Since excess acetic anhydride and benzene do not interfere with bromination of 8-acetylaminoquinoline and serve as solvents, bromination was subsequently effected without isolation of the intermediate 8-acetylaminoquinoline, and the two steps were combined. In this manner, the yield of 5-bromo-8-acetylaminoquinoline can be raised to 85-98.5%.

The acetyl group is split off by heating with hydrochloric acid. The resulting 5-bromo-8-aminoquinoline is diazotized in sulfuric acid solution in presence of alcohol as the reducing agent needed for replacement of the diazo group by hydrogen. With the objective of increasing the yield of 5-bromoquinoline, experiments were run with other reducing agents often employed for this purpose — stannous chloride and hypophosphorous acid [11]. The latter led to considerable resinification of the reaction mixture, and to lowering of the yield of 5-bromoquinoline.

EXPERIMENTAL

Acetylation of 8-aminoquinoline. A solution of 10 g of 8-aminoquinoline in a mixture of 20 ml of benzene and 20 ml of acetic anhydride was refluxed for 30 min.

Bromination of 8-acetylaminoquinoline. Into the above solution (which contained a small, yellowish, crystalline deposit) was run 25 ml of glacial acetic acid with cooling to -2 to 0° in a mixture of ice and salt. In the course of 30 min, with intensive stirring by a mechanical stirrer, 3.5 ml of bromine in 20 ml of glacial acetic acid was slowly added dropwise, while the temperature was held at not higher than 0° . An orange-yellowish precipitate came down. The mixture was diluted with three times its volume of iced water, and made alkaline with NaOH solution to pH 9; some heat was liberated during this operation, and the color of the precipitate became grayish. After complete cooling, the 5-bromo-8-acetylaminoquinoline was filtered, washed on the filter with water, and dried on filter paper. The product had m.p. 137° (the literature gives 140°). Yield 85-92%.

Cleavage of acetyl group from 5-bromo-8-acetylaminoquinoline and replacement of the amino group by hydrogen. A solution of 17 g of 5-bromo-8-acetylaminoquinoline in 150 ml of concentrated hydrochloric acid in a one-liter Erlenmeyer flask was refluxed for 30 min. The mass was cooled to room temperature and diluted with three times its volume of iced water. Bright-red crystals of 5-bromo-8-aminoquinoline hydrochloride came down. After filtration, the precipitate was suspended in a mixture of 175 ml of ethanol and 50 ml of concentrated sulfuric acid, and cooled to 0° in an ice bath. At this temperature (cooling in the ice bath was continued), a solution of 6 g of sodium nitrite in 10 ml of water was slowly added in the course of 20-25 min with intensive stirring. After completion of the addition, the flask was stood for 30 min in the ice bath; the solution turned dark red. To the reaction mixture was then added 5 g of copper powder.* Nitrogen at once started to come off. After the lapse of 25 min, the flask was connected to a reflux condenser and heated on a water bath for about an hour, until evolution of nitrogen ceased. After cooling, the reaction mass was transferred to a two-liter flask; 120-130 ml of 20% sodium hydroxide solution was added (to give an alkaline reaction), and the 5-bromoquinoline was distilled off with steam. Alcohol came over at first and contained approximately $\frac{1}{3}$ of the 5-bromoquinoline. Distillation with steam was continued into the same receiver until the whole of the 5-bromoquinoline had come over (until no further turbidity was observed). At this stage the volume of distillate was one liter. After cooling (3-4 hr), the crystallizing, colorless 5-bromoquinoline was filtered and dried on filter paper at room temperature. M.p. $43-45^{\circ}$ (the literature gives 48°). Yield 40-51%.

This step can be simplified. After decomposition of 5-bromo-8-acetylaminoquinoline with hydrochloric acid, the diazotization of the resulting 5-bromo-8-aminoquinoline can be performed in the same hydrochloric acid medium in presence of the above-mentioned quantity of alcohol and sulfuric acid.

In this somewhat simplified variant, the yields of 5-bromoquinoline are 36-44%.

SUMMARY

A method was developed for preparation of 5-bromoquinoline starting from 8-aminoquinoline. The acetyl derivative of the latter was brominated to 5-bromo-8-acetylaminoquinoline. The acetyl group was then split off and the amino group eliminated via the diazo compound to give 5-bromoquinoline.

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*Very fine copper powder (Merck) was used. It was obtained by reduction of copper in an alcoholic medium. Thin copper turnings result in a much lower yield of 5-bromoquinoline.

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REDUCTION OF NAPHTHOLCARBOXYLIC ACIDS

III. METHYL ESTER OF 2,3-TETRALONECARBOXYLIC ACID

N. M. Przhivalgovskaya, L. N. Lavrishcheva, and V. N. Belov

D. I. Mendeleev Chemical Technological Institute, Moscow

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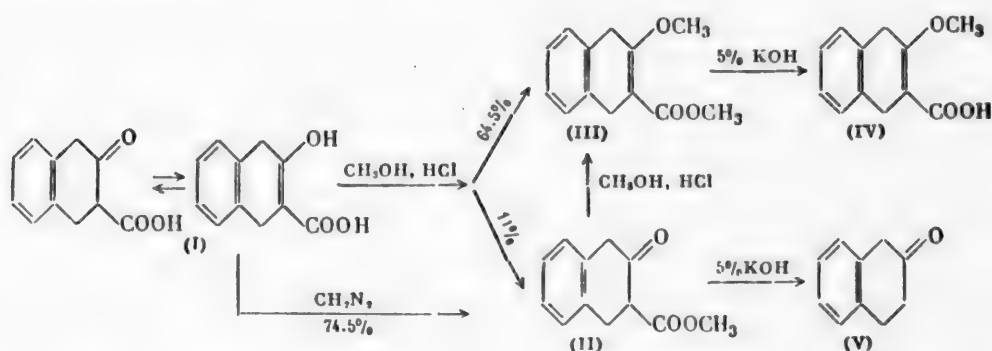
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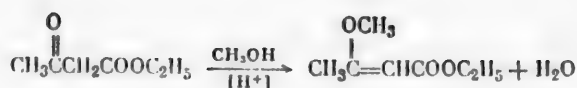
Recently [1], we synthesized 2,3-tetralonecarboxylic acid (I) in quite good yield by the indirect electroreduction of 2,3-naphtholcarboxylic acid. This previously unknown β -keto acid could possess considerable interest as the starting product for the synthesis of various polycyclic compounds, including the heterocyclic type. However, the instability of this acid (it decomposes when heated above 110°, and in aqueous solutions at even lower temperatures, with the formation of β -tetralone and CO₂) complicates its direct use for synthetic purposes.

We worked out a method for the conversion of 2,3-tetralonecarboxylic acid to its methyl ester (II), an entirely stable compound, which may be used for accomplishing syntheses that are characteristic of esters of β -keto acids. We obtained the methyl ester of 2,3-tetralonecarboxylic acid in 74-75% yield by reacting an ether solution of acid (I) with diazomethane. To prove the structure of ester (II), we subjected it to ketonic cleavage, where the expected β -tetralone (V) was obtained.

An attempt to obtain the same ester by the esterification of 2,3-tetralonecarboxylic acid with methyl alcohol in the presence of dry hydrogen chloride revealed that here the main reaction product is the dimethyl ester of the enolic form of 2,3-tetralonecarboxylic acid (III). Only small amounts of the monomethyl ester (II) are formed under these conditions.



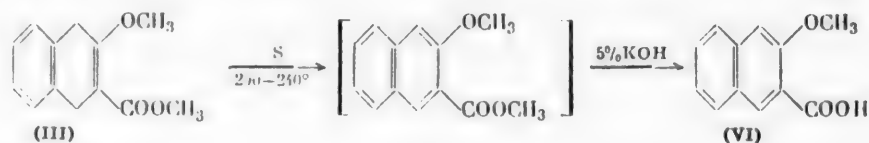
A similar alkylation of the enolic group using alcohol and acid was also observed earlier for compounds that are capable of existing in both the ketonic and the enolic form. Thus, for example, acetoacetic ester under similar conditions smoothly forms the esters of β -hydroxycrotonic acid [2].



We also obtained the methyl ester of 2-methoxy-1,4-dihydro-3-naphthoic acid (III) by reacting the mono-methyl ester of 2,3-tetralonecarboxylic acid (II) with methyl alcohol in the presence of hydrogen chloride. It was established by us that the hydroxyl group in 2,3-hydroxynaphthoic acid or in the methyl ester is not alkylated under such conditions.

The saponification of dimethyl ester (III) gave 2-methoxy-1,4-dihydro-3-naphthoic acid (IV).

To prove the structure of these compounds (III-IV), the methyl ester of 2-methoxy-1,4-dihydro-3-naphthoic acid (III) was dehydrogenated by heating with sulfur at 200-240°, followed by saponification of the obtained product to yield 2-methoxy-3-naphthoic acid (VI).



Acid (VI) had the same melting point as that given in the literature [6].

EXPERIMENTAL

Methyl ester of 2,3-tetralonecarboxylic acid (II). An ether solution of diazomethane (from 90 ml of 40% KOH solution, 300 ml of ether, and 15 g of N-nitrosomethylurea) [3] was added slowly, with mechanical stirring, to a solution of 30 g of 2,3-tetralonecarboxylic acid [recrystallized from CCl_4 , m.p. 110-113° (decomp.)] in 400 ml of ether cooled to 0°. The temperature was kept below 8°. The mixed solutions were allowed to stand overnight in the refrigerator. The next day, the solution was treated with 10 ml of glacial acetic acid (until acid to litmus) to decompose the excess diazomethane. The ether solution was washed with water, then with saturated sodium bicarbonate solution (twice), again with water, and finally it was dried over Na_2SO_4 . The ether was distilled off. The residue in the flask, a yellow-red oil (29.7 g), started to crystallize within a day as coarse tetragonal plates. The crystals were filtered, washed with methyl alcohol, and recrystallized from methanol. Yield 24.1 g (74.5%). M.p. 49°. A solution of the compound in methyl alcohol gives a yellow-green color with aqueous FeCl_3 solution. The compound is soluble in alkali, and decolorizes bromine water.

Found %: C 70.69, 70.84; H 5.68, 5.83. $\text{C}_{12}\text{H}_{12}\text{O}_3$. Calculated %: C 70.63; H 5.92.

2,4-Dinitrophenylhydrazone. Obtained as orange needles (from alcohol); m.p. 163-164°.

Found %: N 14.70, 14.79. $\text{C}_{18}\text{H}_{16}\text{O}_6\text{N}_4$. Calculated %: N 14.58.

Ketonic cleavage. A mixture of 3 g of ester (II) and 25 ml of 5% KOH solution was heated under reflux for 1 hr. The reaction mixture was then acidified and steam distilled. The steam-distilled oil was extracted with ether, the ether solution dried over Na_2SO_4 , the solvent removed by distillation, and the residue was vacuum distilled. Yield 1.7 g (79%). M.p. 99-101° (2 mm), n_D^{20} 1.5597.

2,4-Dinitrophenylhydrazone: m.p. 147-148°. For β -tetralone, b.p. 111-115° (5 mm) [4]; n_D^{20} 1.5594 [5]. The 2,4-dinitrophenylhydrazone has m.p. 147-148° [1]. The mixed melting point was 147-148°.

Methyl ester of 2-methoxy-1,4-dihydro-3-naphthoic acid (III). Method I. Methanol (500 ml) was saturated with dry hydrogen chloride until the weight increase was 90 g. The solution was cooled to room temperature, then 50 g of 2,3-tetralonecarboxylic acid was added, and the whole allowed to stand for two days. After this, the dark reaction mass was poured into 1.5 liters of ice water. The obtained oil was extracted with benzene. The benzene extracts were cooled to 0°, and then treated with cold (-5°) 5% KOH solution (about 10 times) until the test with FeCl_3 was negative. After this, the benzene solution was washed with water and then dried over Na_2SO_4 . The benzene was removed by distillation and the residual oil (45.3 g) was vacuum distilled. The following fractions were obtained: 1st, 120-132° (1 mm), 5.2 g; a mixture of β -tetralone and the diester; 2nd, 132 to 136° (1 mm), 37.1 g; a liquid that quickly crystallized to a solid mass (diester III); and 3rd, 140-190° (12 mm), 1.5 g.

The second fraction was recrystallized twice to give long, coarse crystals with m.p. 59-60°. The reaction with FeCl_3 was negative; also, the compound did not decolorize bromine water.

Found %: C 71.50, 71.53; H 6.63, 6.62. $\text{C}_{13}\text{H}_{14}\text{O}_3$. Calculated %: C 71.52; H 6.47.

The yield of dimethyl ester (III), based on the second fraction, was 64.6%.

The alkaline extracts were poured into 10% acetic acid. The obtained oil was extracted with ether. The ether layer was washed with water, then with saturated NaHCO_3 solution, again with water, and then dried over Na_2SO_4 . Removal of the ether by distillation left 6.05 g of an oil, which crystallized on cooling. The crystals were washed with methyl alcohol. M.p. 46-48°. The mixed melting point with ester (II) was not depressed.

Method II. A solution of 10 g of the methyl ester of 2,3-tetralonecarboxylic acid in 170 ml of methyl alcohol containing 40 g of dry HCl was allowed to stand at room temperature for two days, after which it was poured into 500 ml of ice water. The obtained oil was extracted with benzene. To remove unreacted ester, the benzene extracts were washed several times with 5% KOH solution (until the test with FeCl_3 was negative), then several times with water, and finally dried over Na_2SO_4 . The solvent was removed by distillation, and the residual oil (10.43 g) was vacuum distilled. B.p. 173.5-175° (13 mm), 9.53 g, crystals, m.p. 54-56°. After recrystallization from methyl alcohol, m.p. 59-60°. The mixed melting point with diester (III), obtained from 2,3-tetralonecarboxylic acid, was 59-60°.

2-Methoxy-1,4-dihydro-3-naphthoic acid (IV). A mixture of 2.5 g of diester (III) and 25 ml of 5% KOH was heated for 1.5 hr until complete solution was obtained. The obtained solution (dark-colored) was boiled with activated carbon and filtered. The filtrate was acidified with 10% CH_3COOH . The resulting dark oil crystallized after several hours. The crystals were filtered (1.5 g), and then purified by washing with carbon tetrachloride on a porous plate. Fine white crystals (1.25 g) with m.p. 122-123° were obtained in this manner. The test with FeCl_3 was negative; bromine water was decolorized.

Found %: C 70.61, 70.78; H 6.08, 5.79; acid number 266. $\text{C}_{12}\text{H}_{12}\text{O}_3$. Calculated %: C 70.60; H 5.92; acid number 274.

Dehydrogenation of methyl ester of 2-methoxy-1,4-dihydro-3-naphthoic acid (III). A mixture of 2.5 g of diester (III) and 0.31 g of sulfur in a small flask fitted with a reflux condenser was heated in a metal bath at 200-210° for 2 hr and at 240-250° for 1 hr. After cooling, the reaction mass was dissolved in ether, the ether solution treated with 5% KOH solution to remove acidic products, then washed with water, and finally dried over Na_2SO_4 . The ether was removed by distillation, and the residual oil (2 g) was heated with 20 ml of 5% KOH solution for 1.5 hr, until nearly complete solution had been obtained. The reaction mass was cooled, treated with ether, and the lower (alkaline) layer was acidified with 10% H_2SO_4 . A pale-yellow precipitate was obtained almost immediately. The crystals were filtered and dried in the air. Yield 1.4 g. M.p. 131-133°; after recrystallization from CCl_4 , m.p. 134-135°.

Found %: C 70.85, 70.77; H 4.99, 4.91. $\text{C}_{12}\text{H}_{10}\text{O}_3$. Calculated %: C 71.29; H 4.98. 2-Methoxy-3-naphthoic acid has m.p. 134-135° [6].

SUMMARY

1. A method was developed for the conversion of 2,3-tetralonecarboxylic acid to its methyl ester by reacting the acid with diazomethane in ether solution.
2. It was shown that the main reaction product when 2,3-tetralonecarboxylic acid is esterified with methyl alcohol in the presence of dry hydrogen chloride is the dimethyl ester of the enol form of 2,3-tetralonecarboxylic acid.
3. The structure of the methyl ester of 2,3-tetralonecarboxylic acid was shown by its conversion to β -tetralone, while the structure of the methyl ester of 2-methoxy-1,4-dihydro-3-naphthoic acid was shown by its dehydrogenation with sulfur, followed by saponification to 2-methoxy-3-naphthoic acid.

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MULTINUCLEAR HETEROCYCLIC COMPOUNDS

II. THE STRUCTURE AND COLOR OF SOME 4-PHENYL-DIBENZOYLENEPYRIDINE DERIVATIVES

G. Vanags, É. I. Stankevich, and É. Ya. Gren

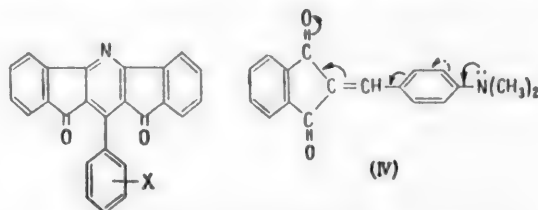
Institute of Organic Chemistry, Academy of Sciences of the LatvSSR

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In previous papers [1,2] we proposed a method for obtaining 4-aryl-2,3,6,5-dibenzoylenepyridines by the reaction of arylideneindandiones with ammonium acetate, and we also elucidated the mechanism of this fairly complex reaction. A more detailed study of 4-phenyl-2,3,6,5-dibenzoylenepyridine (I) and its derivatives was made in the second paper [2]. Some of these compounds show profound changes in color when reacted with either alkali or acid, which is apparently linked with corresponding changes in their structure. The present paper is devoted to a study of the finer structure of these compounds.

It had already been mentioned earlier that yellow or orange 4-phenyl-dibenzoylenepyridines having a hydroxyl group in either the ortho- or the para-position of the phenyl radical are soluble in alcoholic alkalies with either a red or a reddish-violet color, whereas the *m*-hydroxy compound fails to give any deepening of the color when treated with alkalies. Compounds containing the methoxy group prove to be insoluble in alkalies. Using the general procedure, we also synthesized 4-(*p*-dimethylaminophenyl)-2,3,6,5-dibenzoylenepyridine (II). In contrast to all of the other 4-phenyl-dibenzoylenepyridines, this compound is colored dark brown and gives yellow salts when treated with acids. These salts are easily hydrolyzed, which indicates that the original compounds are weak bases. We also synthesized 4-(*p*-dimethylamino-*m*-nitrophenyl)-2,3,6,5-dibenzoylenepyridine (III). This compound is orange-colored and is more difficultly soluble in mineral acids than the preceding.



- (I) X = H; (II) X = *p*-N(CH₃)₂; (III) X = *p*-N(CH₃)₂; *m*-NO₂; (X) X = *o*-OH; (XI) X = *m*-(OH); (XII) X = *o*-OCH₃; (XIII) X = *o*-OH; *m*-OCH₃.

*Original Russian pagination. See C.B. translation.

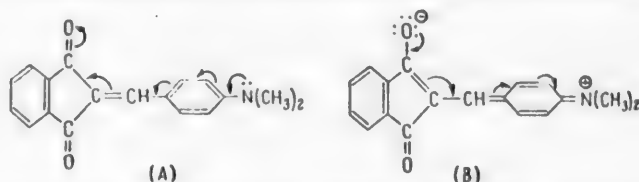
In order to understand the properties and color of these compounds, it is necessary to start with an examination of analogous phenomena existing for the original compounds in this series, namely, the arylideneindandiones, since here we encounter a completely analogous change in the color.

All of the arylideneindandiones used by us to prepare the phenyl-dibenzoylenepyridines were either yellow or orange in color, with the exception of the dark-red *p*-dimethylaminobenzalindandione. A yellow solution of the salt is formed when the latter is dissolved in acid. The salt is unstable and is hydrolyzed with ease when the solution is diluted with water. The compound does not form salts with weak acids, for example, acetic acid, or with very dilute mineral acids, which indicates the weakly basic character of the compound.

Here the electron-donor properties of the dimethylamino group are weakened considerably because of conjugation with the carbonyl groups (IV). Conjugation of the nucleophilic dimethylamino group with the electrophilic carbonyl groups is the reason for the color of the mentioned compound.

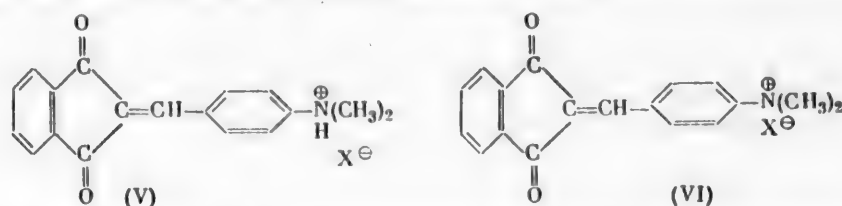
The absorption spectra of *p*-dimethylaminobenzalindandione and many other arylideneindandiones were studied by Radulescu and Georgescu [3]. Whereas, for most benzalindandiones, the absorption maxima are located in the ultraviolet region at 350-375 m μ , in the case of *p*-dimethylaminobenzalindandione the absorption of light occurs even in the visible region ($\lambda_{\max} = 500 \text{ m}\mu$).

To be sure, in connection with the mutual effect of the dimethylamino and carbonyl groups, the distribution of the electron density in the dimethylaminobenzalindandione changed, and the above-given formula (IV) no longer reflects its structure. Without a doubt, the molecule acquired a more polar character, and it must be assumed, as had already been indicated by Brooker [4], that the correct structure with a true distribution of the electron density will occupy an intermediate position between the two possible extreme structures (A) and (B).



As is known, the phenomenon of solvatochromism makes it possible at times to judge as to the bipolar structure of molecules [5,6]. A study of the solvatochromism of *p*-dimethylaminobenzalindandione (IV) reveals that its electronic density is closer to the nonionic structure (A) than to the intralindionid structure (B), which could have been expected, since the energy of (B) is greater than the energy of (A) [4].

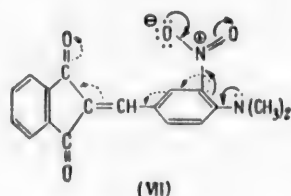
The structure of the *p*-dimethylaminobenzalindandione salt apparently resembles the structure of the benzalindandione, because for the salt $\lambda_{\max} = 350 \text{ m}\mu$ [3]. This could be expected, since both the nucleophilic properties of the dimethylamino group and the color disappear when the salt is formed; the distribution of the electron density for a salt like (V) is the same as for the benzalindandione.



It is for exactly the same reason that the trimethylammonium derivative of benzalindandione (VI) is nearly colorless, because the introduction of still another methyl group in the dimethylamino group results in liquidation of its nucleophilic character [7]. The disappearance of color when the dimethylamino group is alkylated has also been observed for compounds of the betaine type [8].

A hypsochromic effect is observed when a nitro group is also introduced into the *p*-dimethylaminobenzalindandione molecule (IV). *p*-Dimethylamino-*m*-nitrobenzalindandione is colored orange-yellow. The nitro group, found in series with the dimethylamino group, influences the latter, and a new electron-donor-acceptor system is formed: $\text{N}(\text{CH}_3)_2\text{-NO}_2$. As a result of this interaction, the nucleophilic properties of the dimethylamino group are weakened substantially, and its influence on the carbonyl groups is slight. For this reason,

p-dimethylamino-m-nitrobenzalindandione is colored orange-yellow, and its most probable structure is that of (VII).



Some of the o- and p-hydroxybenzalindandiones in either alcoholic caustic or methyrate solution also give red or violet-red solutions, with maximum absorption at 500-550 mμ [3,9], whereas in alcohol solution without the caustic, $\lambda_{\max} \approx 400$ mμ. It is obvious that also here the real structure must be sought between the two extreme structures (C) and (D).

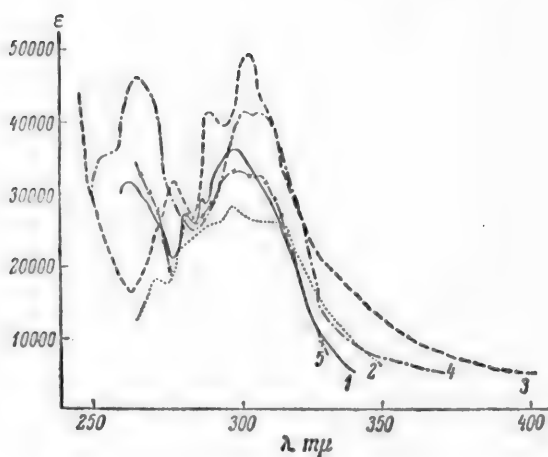
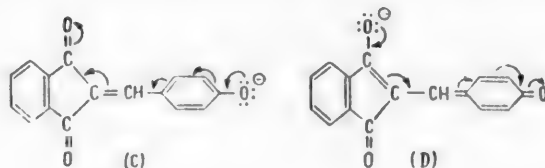


Fig. 1. Ultraviolet spectra of phenyl-dibenzoylenepyridines. 1) (I), $0.25 \cdot 10^{-4}$ M, in dioxane; 2) (X), $0.25 \cdot 10^{-4}$ M, in dioxane; 3) (X), $0.25 \cdot 10^{-4}$ M, in $C_2H_5OH + C_2H_5ONa$; 4) (XI), $0.25 \cdot 10^{-4}$ M, in $C_2H_5OH + C_2H_5ONa$; 5) (XI), $0.25 \cdot 10^{-4}$ M, in dioxane.

Only a solution of 4-(p-dimethylaminophenyl)-dibenzoylenepyridine (II) in concentrated hydrochloric acid gives a slight hypsochromic shift of 15-20 mμ (Fig. 2).

In contrast, the less well-defined maxima at the boundary of the ultraviolet region and the visible portion ($\epsilon = 4000-8000$) show marked change as a function of both the substituent and the medium. 4-Phenyl-dibenzoylenepyridine, having the least nucleophilic substituent H, still absorbs in the ultraviolet region ($\lambda_{\max} = 380$ mμ, Fig. 3), whereas the absorption maximum of 4-(p-dimethylaminophenyl)-dibenzoylenepyridine is already found in the visible portion (420 mμ), in which connection the drop in the curve is also gentle on the side of the longer wavelengths (the electron-donor properties of the dimethylamino group are sufficiently great to cause a change in the distribution of the electron density in the molecule). The same as in the case of the p-dimethylamino-benzalindandione, the actual structure must be sought between the two most energetically favorable structures (E) and (F).

A similar color is not observed for the m-hydroxybenzalindandione, because here the reaction of the hydroxyl group with the carbonyl is much weaker.

The above discussion can also be applied in its entirety to the corresponding 4-phenyl-dibenzoylenepyridines, except that here the changes in the spectra are not as sharply defined. Although this is not strange, still the absorption spectra of all of the phenyl-dibenzoylenepyridines in the ultraviolet region are practically the same, independent of the medium or of the substituents (Figs. 1 and 2).

All of the phenyl-dibenzoylenepyridines exhibit a sharply defined maximum at about 300 mμ; in addition, for some of them, an absorption band is also observed at 260-270 mμ. It is possible that the maximum of the shorter wavelengths is also characteristic for all of the phenyl-dibenzoylenepyridines, but is found somewhat further in the ultraviolet region; we were unable to detect it because of the absorption of the solvent, dioxane.

These two maxima ($\epsilon = 20,000-40,000$) are hardly affected by either the substituent or the medium.

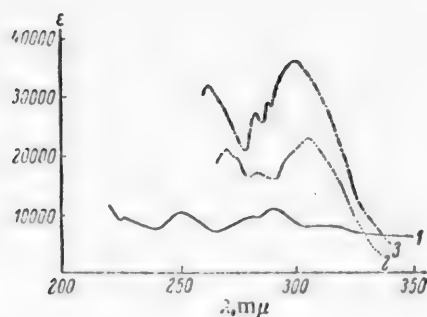


Fig. 2. Ultraviolet spectra of 4-(p-dimethylaminophenyl)-dibenzoylenepyridine in dioxane and in concentrated hydrochloric acid. 1) (II), $1 \cdot 10^{-4}$ M, in conc. HCl; 2) (II), $0.5 \cdot 10^{-4}$ M, in dioxane; 3) (I), $0.25 \cdot 10^{-4}$ M, in dioxane.

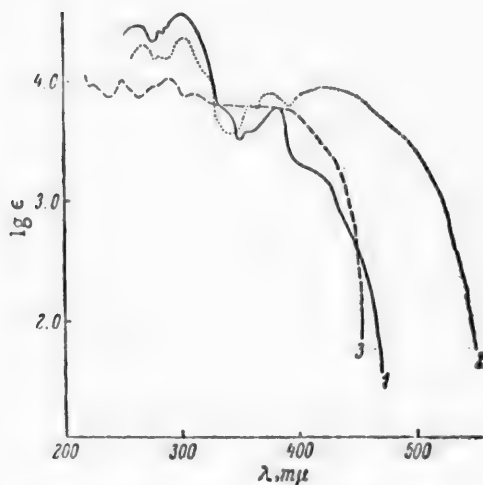
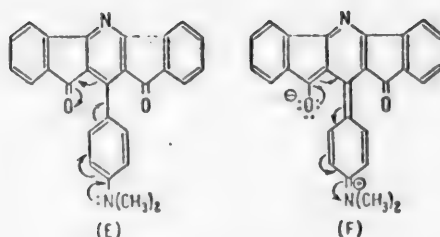
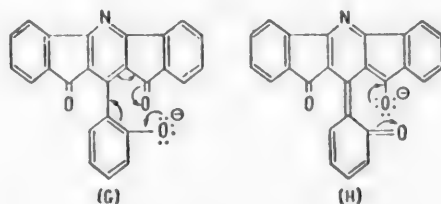


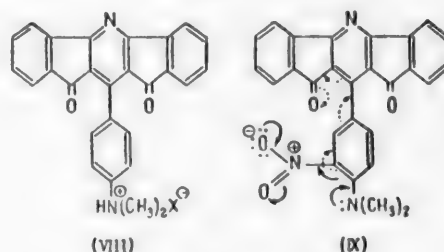
Fig. 3. Absorption spectra of 4-phenyl-dibenzoylenepyridine and 4-(p-dimethylaminophenyl)-dibenzoylenepyridine in the ultraviolet and in the visible region. 1) (I), $0.25 \cdot 10^{-4}$ M, in dioxane; 2) (II), $0.5 \cdot 10^{-4}$ M, in dioxane; 3) (II), $1 \cdot 10^{-4}$ M, in conc. HCl.

dine in sodium ethylate solution gives a maximum at about 500 mμ, which is shifted toward longer wavelengths by 80 mμ when compared with 4-(p-dimethylaminophenyl)-dibenzoylenepyridine (Fig. 4). Also, in this case, it is possible to depict the existence of two forms (G) and (H), between which the actual structure with a real distribution of the electron density is found.



The salt, whose color and spectrum resemble that of 4-phenyl-dibenzoylenepyridine, can be assigned structure (VIII).

4-(p-Dimethylamino-m-nitrophenyl)-dibenzoylenepyridine (III), in contrast to the dark-brown 4-(p-dimethylaminophenyl)-dibenzoylenepyridine (II), is colored orange-yellow. This could be expected, since the nitro group interferes with the conjugation between the dimethylamino group and the carbonyl group, in the same manner as has already been described for the corresponding benzalindandiones (IV, VII). As a result of this, the deep color disappears, and the structure of 4-(p-dimethylamino-m-nitrophenyl)-dibenzoylpyridine is close to that of the nonionic form (IX).



In sodium ethylate solution, 4-(o-hydroxyphenyl)-dibenzoylenepyridine (X) has a substituent with greater electron-donor properties than that possessed by the p-dimethylamino group and, specifically, $-\text{O}^-$, and consequently an even greater bathochromic shift of the absorption band than in the case of the dimethylamino group could be expected.

Actually, 4-(o-hydroxyphenyl)-dibenzoylenepyri-

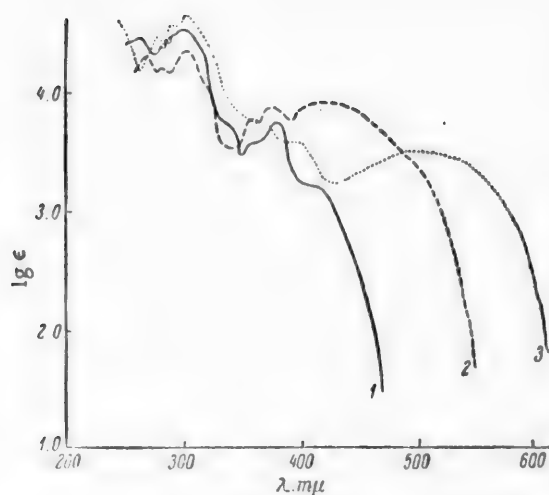


Fig. 4. Absorption spectra of 4-(p-dimethylamino-phenyl)-dibenzoylenepyridine in dioxane and of 4-(o-hydroxyphenyl)-dibenzoylenepyridine in alcoholate. 1) (I), $0.25 \cdot 10^{-4}$ M, in dioxane; 2) (II), 0.5×10^{-4} M, in dioxane; 3) (X), $0.25 \cdot 10^{-4}$ M, in $C_2H_5OH + C_2H_5ONa$.

posited after the lapse of some time. Toward the end of reaction the mixture was treated with 3-4 ml of perhydrol, and the whole was then refluxed for several minutes. The dark-red solution turned orange, and yellow crystals of 4-(m-hydroxyphenyl)-2,3,6,5-dibenzoylenepyridine deposited. The reaction mixture was cooled, and the precipitate was filtered and washed with a little acetic acid. Yield 0.87 g (44%). After recrystallization from dioxane, the melting point was around 390° (block) (with decomp.). The compound is readily soluble in dioxane, difficultly soluble in toluene, and insoluble in alcohol and in ether; it is insoluble in aqueous alkalies, but is readily soluble in alcoholic caustic or ethylate (with a yellow color). Gradual hydrolysis occurs when the alcoholic solution is diluted with a large volume of water, and the compound precipitates unchanged.

Found %: N 3.47. $C_{25}H_{13}O_3N$. Calculated %: N 3.73.

4-(o-Methoxyphenyl)-2,3,6,5-dibenzoylenepyridine (XII). A mixture of 4.1 g of o-methoxybenzalindandione [13], 24 g of ammonium acetate (20-fold excess), and 75 ml of glacial acetic acid was refluxed for 20 min, then oxidized with hydrogen peroxide, and the yellow crystals of 4-(o-methoxyphenyl)-2,3,6,5-dibenzoylenepyridine were separated. Yield 1.5 g (49.5%). After recrystallization from xylene, m.p. $310-315^\circ$ (block). The compound is readily soluble in dioxane, less readily soluble in benzene and glacial acetic acid, and insoluble in ether; it is insoluble in both aqueous and alcoholic alkalies, and also in sodium ethylate solution.

Found %: N 3.79. $C_{26}H_{15}O_3N$. Calculated %: N 3.60.

4-(o-Hydroxy-m-methoxyphenyl)-2,3,6,5-dibenzoylenepyridine (XIII). A mixture of 2.75 g of o-hydroxy-m-methoxybenzal-1,3-indandione [14], 15.1 g of ammonium acetate, and 100 ml of glacial acetic acid was refluxed for 30 min, and then the dark-yellow crystals of 4-(o-hydroxy-m-methoxyphenyl)-2,3,6,5-dibenzoylenepyridine were separated. Yield 1 g (50%). After recrystallization from dioxane the melting point was about 340° (block). The compound is readily soluble in dioxane, less readily soluble in toluene, difficultly soluble in glacial acetic acid, and insoluble in alcohol and in ether; it is also insoluble in aqueous alkalies, but does dissolve in alcoholic caustic or in ethylate solution with a red-violet color. The original product can be precipitated by acidification of the solution or by simple dilution with water.

Found %: N 3.70. $C_{26}H_{15}O_4N$. Calculated %: N 3.46.

As had already been mentioned, a deepening of the color is not observed when 4-(m-hydroxyphenyl)-dibenzoylenepyridine (XI) is treated with alkali. This indicates that a transformation similar to the preceding is not possible in this case.

In Fig. 4 it can be seen that the band of the long waves shows bathochromic shift if nucleophilic substituents are introduced into the molecule, in which connection the magnitude of shift depends on the ease with which the substituent can donate electrons, and falls into the following order: $-H$, $-N(CH_3)_2$, $-O^-$. All of this is in complete accord with theoretical considerations. The only thing that is still not clear at the present time is why a change in the configuration of the electrons is without effect on the band of the short waves, nevertheless, cases similar to this are known [10,11].

EXPERIMENTAL

4-(m-Hydroxyphenyl)-2,3,6,5-dibenzoylenepyridine (XI). A mixture of 2.62 g of m-hydroxybenzal-1,3-indandione [12], 16.2 g of ammonium acetate (20-fold excess), and 80 ml of glacial acetic acid was heated under reflux for 20 min. The solution soon became dark red, and yellow crystals de-

4-(p-Dimethylaminophenyl)-2,3,6,5-dibenzoylenepyridine (II). A mixture of 3.22 g of p-dimethylamino-benzalindandione [13], 17.4 g of ammonium acetate, and 75 ml of glacial acetic acid was refluxed for 1.5 hr. Dark-brown crystals of 4-(p-dimethylaminophenyl)-2,3,6,5-dibenzoylenepyridine deposited. Yield 0.62 g (27%). Oxidation with hydrogen peroxide failed to increase the yield. After recrystallization from nitrobenzene, and boiling the precipitate with either dioxane or alcohol, the melting point was about 300° (block). The compound sublimes readily.

Found %: N 7.04. $C_{27}H_{18}O_2N_2$. Calculated %: N 6.96.

The compound is readily soluble in nitrobenzene and in benzyl acetate, less readily soluble in dioxane, difficultly soluble in carbon tetrachloride and decalin, and insoluble in ethyl and butyl alcohols, in acetone, and in ether; it is insoluble in alkalis and in sodium ethylate solution, but is readily soluble in concentrated sulfuric, hydrochloric, nitric, and phosphoric acids with the formation of yellow solutions. At times solution also occurs in more dilute acids, and even in 2 N sulfuric acid. If the solutions in concentrated acids are diluted with water, then the yellow salt precipitates; the latter hydrolyzes on standing, and the precipitate again assumes a brown color.

The phenomenon of solvatochromism is characteristic for the 4-(p-dimethylamino)-dibenzoylenepyridine: in nonpolar solvents, for example, in carbon tetrachloride or decalin, it dissolves with a yellow color, and in benzene or dioxane it dissolves with an orange color, but in polar solvents like nitrobenzene and benzyl alcohol it dissolves with a red color. The liquid becomes lighter in color when reduced with zinc dust in glacial acetic acid, and a blue fluorescence appears. Dilution with water fails to give a precipitate.

Hydrochloride. A mixture of 0.5 g of the 4-(p-dimethylaminophenyl)-dibenzoylenepyridine and 200 ml of concentrated hydrochloric acid was heated on the water bath until solution was obtained. The yellow solution was filtered and evaporated on the water bath with frequent mixing of the solution. The evaporation was stopped when 20-30 ml of liquid remained. The yellow crystals were separated and washed with a little concentrated hydrochloric acid. Yield of 4-(p-dimethylaminophenyl)-dibenzoylenepyridine hydrochloride 0.46 g (84%). Hydrogen chloride is evolved when the salt is heated, and the residue is the brown 4-(p-dimethylaminophenyl)-dibenzoylenepyridine with melting point around 360° (block). In organic solvents and in water the salt decomposes to the free base and hydrogen chloride. The salt dissolves in glacial acetic acid without decomposition (with a yellow color), but we were unable to recrystallize it in this manner. The salt can also be obtained by passing dry hydrogen chloride into a suspension of the free base in dioxane or some other solvent, but then it is not obtained in crystalline form.

Found %: N 5.99. $C_{27}H_{18}O_2N_2 \cdot HCl$. Calculated %: N 6.38.

4-(p-Dimethylamino-m-nitrophenyl)-2,3,6,5-dibenzoylenepyridine (III). A mixture of 3.21 g of p-dimethylamino-m-nitrobenzalindandione [15], 15.4 g of ammonium acetate, and 120 ml of glacial acetic acid was refluxed for 30 min, then oxidized with hydrogen peroxide, and the orange crystalline precipitate of 4-(p-dimethylamino-m-nitrophenyl)-2,3,6,5-dibenzoylenepyridine was separated by filtration. Yield 0.6 g (27%). After recrystallization from dioxane the melting point was around 400° (block). The compound is readily soluble in dioxane, difficultly soluble in benzene and glacial acetic acid, and insoluble in alcohol and in ether; it is comparatively soluble in concentrated mineral acids (with a yellow color), but to a lesser degree than 4-(p-dimethylaminophenyl)-dibenzoylenepyridine.

Found %: N 9.13. $C_{27}H_{17}O_4N_3$. Calculated %: N 9.40.

SUMMARY

Based on a study of the absorption spectra of some 4-phenyl-2,3,6,5-dibenzoylenepyridine derivatives, an opinion was expressed regarding the finer structure of these compounds, and the dependence of their color and chemical properties on the structure was discussed.

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CHEMISTRY OF SELENOPHENE

XXVI. 2-CYCLOPROPYLSELENOPHENE AND 2-PROPENYLSELENOPHENE

Yu. K. Yur'ev, N. N. Mezentsova, and V. E. Vas'kovskii

Moscow State University

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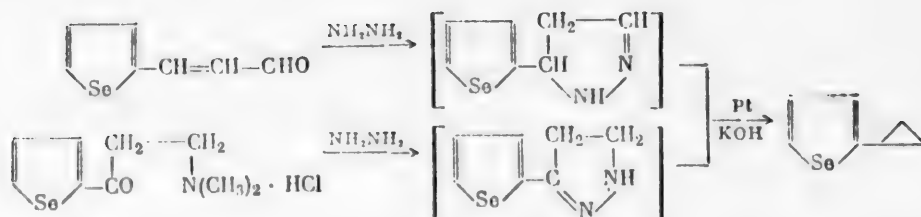
In a previous paper [1], we reported that the formylation of 2-vinylselenophene with dimethylformamide yields β -(2-selenienyl)acrolein. However, since this synthesis path presents some difficulties, we report in the present paper the synthesis of the same compound by the condensation of 2-selenophenecarboxaldehyde with acetaldehyde in the presence of alkali.

We reacted β -(2-selenienyl)acrolein with hydrazine hydrate, but here we were unable to isolate the resulting 5-(2-selenienyl)pyrazoline in the pure state because, even when vacuum distilled, the compound decomposes to a large degree, with the formation of 2-cyclopropylselenophene. We obtained 2-cyclopropylselenophene (2-selenienylcyclopropane) when 5-(2-selenienyl)pyrazoline was decomposed by the general method of N. M. Kizhner.

Judging from the constants, the obtained 2-cyclopropylselenophene contained the 2-selenienylalkene as impurity, which, of necessity, should have been formed in the Kizhner decomposition of the 5-(2-selenienyl)pyrazoline.

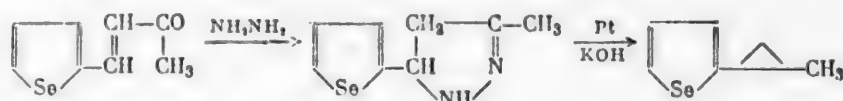
2-Cyclopropylselenophene was also synthesized from 2-(β -dimethylaminopropyl)selenophene hydrochloride [2] by reacting the latter with hydrazine hydrate and subsequent decomposition of the formed 5-(2-selenienyl)pyrazoline by the above-indicated method. This method of obtaining 2-cyclopropylselenophene is simpler and more convenient.

* Original Russian pagination. See C.B. translation.



Removal of the 2-selenienylalkene impurity from the compounds was accomplished by treating them with potassium permanganate solution and subsequent reaction with 2,4-dinitrobenzenesulfonyl chloride.

In contrast to the monosubstituted pyrazoline, the disubstituted pyrazoline 3-methyl-5-(2-selenienyl)pyrazoline, obtained by the condensation of selenenalacetone with hydrazine hydrate, was a stable compound and could be vacuum distilled without decomposition. 1-Phenyl-5-(2-selenienyl)pyrazoline was obtained by the condensation of 2-selenenalacetone with phenylhydrazine, and melted without decomposition. The decomposition of 3-methyl-5-(2-selenienyl)pyrazoline by the Kizhner method gave 2-(2-methylcyclopropyl)selenophene [1-methyl-2-(2-selenienyl)cyclopropane]. Its purification from a small amount of 2-selenienylbutene was accomplished as indicated above.



The ultraviolet absorption spectra (taken in methanol using an SF-4 spectrophotometer) of 2-cyclopropylselenophene and 2-(2-methylcyclopropyl)selenophene (like the ultraviolet absorption spectra of other selenophene homologs [6]), fail to show any differences in the electron transitions (2500 Å): λ_{\max} 248 m μ , log ϵ 4.08, and λ_{\max} 250 m μ , log ϵ 4.01, respectively.

EXPERIMENTAL

β -(2-Selenienyl)acrolein. Thirty grams of 2-selenophenecarboxaldehyde was added in drops, with vigorous stirring, to 400 ml of 5% NaOH solution, and then a solution of 20 g of acetaldehyde in 20 ml of water was added in 5 hr to the obtained emulsion with ice-water cooling. The reaction product was extracted with ether; the extracts were washed with water and then dried over magnesium sulfate. Removal of the ether by distillation and vacuum distillation of the residue gave 10 g of unchanged aldehyde and 16.5 g of β -(2-selenienyl)acrolein (71.5%, based on consumed 2-selenophenecarboxaldehyde).

B.p. 128-129° (2 mm), n_D^{20} 1.6995, d_4^{20} 1.5487, M_R 46.16. $C_7H_6OSeF_3$. Calculated %: C 41.59.

Literature data [1]: b.p. 155-155.5° (15 mm), n_D^{20} 1.7006, d_4^{20} 1.5495.

Oxime. A mixture of 1.85 g of β -(2-selenienyl)acrolein, 1.4 g of hydroxylamine hydrochloride, and 2.8 g of potassium carbonate in 7 ml of water and 15 ml of alcohol was heated for 3 hr. We obtained 1.9 g (95% yield) of product as white crystals with m.p. 152-153° (from 50% alcohol).

Found %: C 42.30, 42.37; H 3.67, 3.79; Se 39.12, 39.19. C_7H_7ONSe . Calculated %: C 42.02; H 3.53; Se 39.40.

Phenylhydrazone. A mixture of 8 g of β -(2-selenienyl)acrolein in 150 ml of water, and 8 g of phenylhydrazine hydrochloride and 20 g of sodium acetate in 100 ml of water was shaken for 1 hr. We obtained 11.5 g (96% yield) of product as colorless crystals with m.p. 151-152° (with decomp., from methyl alcohol).

Found %: C 56.48, 56.55; H 4.20, 4.27; Se 28.68, 28.60. $C_{13}H_{12}N_2Se$. Calculated %: C 56.73; H 4.39; Se 28.69.

1-Phenyl-5-(2-selenienyl)pyrazoline. A solution of 2 g of β -(2-selenienyl)acrolein phenylhydrazone in 10 ml of glacial acetic acid was heated for 1 hr on the water bath and then diluted with 25 ml of water. We obtained 1.4 g (70% yield) of product as pale-brown needle crystals with m.p. 92-93° (from aqueous methyl alcohol).

Found %: C 56.68, 56.70; H 4.53, 4.43; Se 28.41, 28.37. $C_{13}H_{12}N_2Se$. Calculated %: C 56.73; H 4.39; Se 28.69.

3-Methyl-5-(2-selenienyl)pyrazoline. A solution of 12.5 g of 2-selenenalacetone (b.p. 138-139° at 5 mm, n_D^{20} 1.6578, d_4^{20} 1.4632 [3]) in 30 ml of alcohol was added with vigorous stirring to 15 ml of hydrazine hydrate, and the mixture was heated on the water bath for 1 hr; the alcohol and excess hydrazine hydrate were distilled off up to 140°, and then in vacuo. The residue was dissolved in ether and the solution was dried over potassium carbonate. After removal of the ether by distillation the residue was vacuum distilled in a nitrogen stream. We obtained 11.9 g (89% yield) of product.

B.p. 129-130° (2 mm), n_D^{20} 1.6010, d_4^{20} 1.4607, M_R^D 50.01. $C_8H_{10}N_2SeF_3$. Calculated 50.23.*

Found %: C 44.70, 44.90; H 4.73, 4.89. $C_8H_{10}N_2Se$. Calculated %: C 45.08; H 4.72.

2-(2-Methylcyclopropyl)selenophene. To the 3-methyl-5-(2-selenienyl)pyrazoline, obtained as described above from 20 g (0.1 mole) of 2-selenenalacetone, and contained in a flask fitted with a reflux condenser, were added 1 g of KOH, fused in a silver crucible, and a small amount of platinized carbon, after which the whole was heated in an oil bath at 200-210° for 40 min. Then the fraction distilling up to 82° at 11 mm was collected (about 15 g), which was then steam-distilled; the steam distillate was extracted with ether and the extract was dried over calcium chloride. After distilling off the ether, the residue was vacuum distilled. We obtained 13.7 g (74% yield, based on 2-selenenalacetone) of product: b.p. 86-87° (13 mm), n_D^{20} 1.5620, d_4^{20} 1.3352.

Removal of the selenienylalkene impurity was accomplished by the method of R. Ya. Levina and co-workers [5]: A mixture of 7.4 g (0.04 mole) of 2-(2-methylcyclopropyl)selenophene, 8 ml of glacial acetic acid, and 0.84 g (0.004 mole) of 2,4-dinitrobenzenesulfonyl chloride was heated on the boiling water bath for 1 hr. The next day, the acetic acid and purified compound were vacuum distilled; the distillate was diluted with water (1:2) and then extracted with ether; the ether extract was washed with 2 N KOH solution, then with water, and dried over calcium chloride. Removal of the ether by distillation gave 6.7 g (90%) of 2-(2-methylcyclopropyl)selenophene:

B.p. 74-75° (8 mm), n_D^{20} 1.5614, d_4^{20} 1.3358, M_R^D 44.92. $C_8H_{10}SeF_2\Delta$. Calculated: 45.16.

Found %: C 52.12, 52.10; H 5.40, 5.50; Se 42.35, 42.29. $C_8H_{10}Se$. Calculated %: C 51.90; H 5.41; Se 42.60.

2-Cyclopropylselenophene. a) From 14 g (0.076 mole) of β -(2-selenienyl)acrolein and 18 ml of hydrazine hydrate in 30 ml of alcohol, after decomposition of the obtained 5-(2-selenienyl)pyrazoline as described above, we obtained 5.7 g (44%) of product: b.p. 76-77° (15 mm), n_D^{20} 1.5822.

b) A mixture of 25 g (0.14 mole) of 2-acetoselenophene, 15.5 g (0.19 mole) of dimethylamine hydrochloride, 5.5 g of paraform, and 25 ml of alcohol was heated for 2 hr on the boiling water bath. Then 40 ml of methyl alcohol and 15 ml of water were added, and the obtained solution was added in drops, with stirring, to 12 ml of 40% NaOH in 25 ml of methyl alcohol at 40-50°, followed by heating the mixture on the water bath for 15 min. The solvents and unchanged hydrazine hydrate were vacuum distilled, and the residue was extracted with ether; the ether extracts were dried over potassium carbonate. The ether was distilled off and the residue [3-(2-selenienyl)pyrazoline] was decomposed as described above. We obtained 11 g (44.5%) of product: b.p. 80-81° (19 mm), n_D^{20} 1.5768.

After purification of 5.5 g of the compound by treatment with 0.7 g of 2,4-dinitrobenzenesulfonyl chloride in 6 ml of glacial acetic acid (as described above), we obtained 4.6 g (84%) of 2-cyclopropylselenophene.

B.p. 71-72° (13 mm), n_D^{20} 1.5751, d_4^{20} 1.4046, M_R^D 40.25. $C_7H_8SeF_2\Delta$. Calculated: 40.54.

Found %: C 48.96, 48.74; H 4.87, 4.89; Se 46.01, 45.93. C_7H_8Se . Calculated %: C 49.13; H 4.71; Se 46.22.

2-Propenylselenophene. Twenty grams of ethyl(2-selenienyl)carbinol (b.p. 110° (8 mm), n_D^{20} 1.5669, d_4^{20} 1.4507; obtained from 20 g of 2-selenophenecarboxaldehyde, 16 g of ethyl bromide, and 3.4 g of magnesium [1]) was heated in a Claisen flask with potassium bisulfate; the fraction boiling at 70-72° (9 mm) was collected; this fraction was dried over magnesium sulfate; the ether was vacuum distilled. We obtained 12 g (70%) of product.

* The refractive constant for the -N-NH group was taken equal to 5.78 [4].

B.p. 82-82.5° (18 mm), n_D^{20} 1.6075, d_4^{20} 1.3894, M_R 42.55. $C_7H_5SeF_3$. Calculated: 41.53; EM_D 0.97.
 Found %: C 48.88, 48.72; H 4.63, 4.57; Se 45.90, 45.81. C_7H_5Se . Calculated %: C 49.13; H 4.71; Se 46.22.

SUMMARY

1. The condensation of 2-selenophenecarboxaldehyde with acetaldehyde in the presence of alkali yields β -(2-selenienyl)acrolein.
2. The decomposition of 5- or 3-(2-selenienyl)pyrazoline, and also of 3-methyl-5-(2-selenienyl)pyrazoline, by the general method of Kizimer, yields 2-cyclopropylselenophene and 2-(2-methylcyclopropyl)-selenophene, respectively.
3. The dehydration of ethyl(2-selenienyl)carbinol yields 2-propenylselenophene.

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CATALYTIC OXIDATION OF ALIPHATIC AMINES WITH HYDROGEN PEROXIDE

O. L. Lebedev and S. N. Kazarnovskii

Gor'kii Polytechnical Institute

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As we had reported in a previous paper, the mild oxidation of cyclohexylamine with hydrogen peroxide in the presence of sodium tungstate and trilon B yields cyclohexanone oxime [1]. It was interesting to study the oxidation of other aliphatic amines and elucidate the rules governing the reaction.

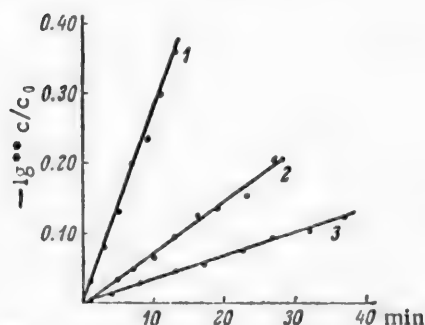


Fig. 1. Kinetics of the oxidation of methylamine (1), ethylamine (2), and isopropylamine (3) with pertungstate.

The oxidation of aliphatic amines in dilute aqueous solution comes closest to being a second-order reaction: The rate of the reaction is directly proportional to the product of the amine and sodium tungstate concentrations (Table 1). The catalyst is found in the solution as pertungstate, the concentration of which does not change during reaction because of an excess of hydrogen peroxide. For this reason, the reaction will be described by the equation $\ln \frac{c}{c_0} = -k [\text{sodium tungstate}] \tau$, where c_0 is the initial concentration of the amine (mole/liter), c is the amine concentration at time τ , and k is the second-order reaction constant (liter per mole per sec).

In the case where the oxidation was run without catalyst, the constant was determined using the equation $\ln \frac{c}{c_0} = -0.30k\tau$,

*Original Russian pagination. See C.B. translation.

**As in original — Publisher.

TABLE 1

Effect of Change in the Concentration of Sodium Tungstate, Amine, and Hydrogen Peroxide on the Oxidation Rate of the Amine (Experimental Conditions are Given in "Experimental")

Name of oxidized amine	Change in oxidation rate of amine with change in amount of component:		
	4-fold inc. in amt. of sodium tungstate	2-fold inc. in amt. of amine	2-fold inc. in amt. of hydrogen peroxide
Cyclohexylamine	3.9	2.1	1.0
Morpholine	4.0	1.8	1.0
Diethylamine	3.8	2.1	0.7
Triethylamine	3.7	2.1	1.0
tert-Amylamine	4.0	—	—

TABLE 2

Reaction Rate Constants for the Oxidation of Amines

Expt. No.	Amine	K	Expt. No.	Amine	K
1	Methylamine	0.25		(Alcohol-water)	
2	Dimethyl-	0.96	32	Trimethyl-	0.12
3	Trimethyl-	1.00	33	Diethyl-	0.11
4	Ethyl-	0.070	34	Triethyl-	0.014
5	Diethyl-	0.26	35	Di-n-butyl-	0.063
6	Triethyl-	0.068	36	Diisobutyl-	0.063
7	n-Propyl-	0.075	37	Tri-n-butyl	0.0037
8	Di-n-propyl-	0.26	38	Cyclohexyl-	0.010
9	Isopropyl-	0.031	39	Dicyclohexyl-	0.011
10	Diisopropyl-	0.042	40	Piperidine	0.24
11	n-Butyl-	0.075		(Sodium molybdate, water)	
12	tert-Butyl-	0.011	41	Methyl-	0.021
13	tert-Amyl-	0.012	42	Dimethyl-	0.089
14	Cyclohexyl-	0.042	43	Trimethyl-	0.083
15	Ethanol-	0.11	44	Diethanol-	0.17
16	Diethanol-	1.27	45	Triethanol-	0.061
17	Triethanol-	0.28		(Without catalyst, water)	
18	Morpholine	0.47	46	Dimethyl-	$0.77 \cdot 10^{-4}$
19	Piperidine	0.60	47	Trimethyl-	$6.5 \cdot 10^{-4}$
20	Hexamethylenediamine	1.08	48	Triethyl-	$1.8 \cdot 10^{-4}$
21	Ammonia	0.0011	49	Diethanol-	$0.52 \cdot 10^{-4}$
22	Benzylamine	0.084	50	Triethanol-	$2.7 \cdot 10^{-4}$
23	Aniline	0.1		(Without catalyst, alcohol-water)	
24	Glycine, Na salt	0.047	51	Trimethyl-	$0.77 \cdot 10^{-4}$
25	Alanine, Na salt	0.021	52	Tri-n-butyl-	$0.20 \cdot 10^{-4}$
26	ϵ -Aminocaproic acid, Na salt	0.056			
27	Hydrazine	0.5			
28	Ethylenediamine	0.14			
29	Hexamethylenediamine	0.075			
30	Hydroxylamine	0.037			
31	2,2,6,6-Tetramethylpiperidine	0.0078			

where 0.30 is the average concentration of the hydrogen peroxide (in mole/liter) during reaction. The character of the experimental curves is shown in Fig. 1. Using similar plots, we determined the reaction rate constants for all of the amines listed in Table 2 and plotted in Fig. 2.

The shape of the curves in Fig. 2 can be explained by assuming that the rate with which all aliphatic amines and ammonia oxidize is determined by the influence of two factors, namely the affinity of the nitrogen atom toward the peroxide oxygen atom attacking it, and the magnitude of the steric hindrance obstructing the path of the oxidizing agent in its approach to the nitrogen atom. The affinity of the nitrogen atom of the amine

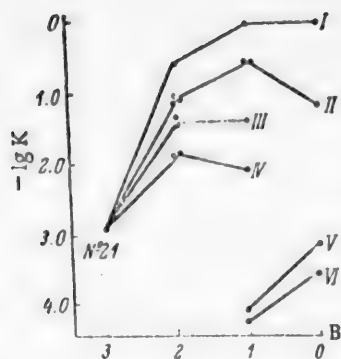


Fig. 2. Relation between the oxidation rate constant and the structure of amines: The B axis represents the number of hydrogen atoms attached to the nitrogen of the amine (3 designates NH_3 , 2, RNH_2 , 1, R_2NH , and 0, R_3N). I) Ammonia and methylamines $(\text{CH}_3)_{0-3}\text{NH}_{3-0}$. The curve represents expt. nos. 21, 1, 2, and 3 (Table 2). II) Amines $(\text{RCH}_2)_{0-3}\text{NH}_{3-0}$; expt. nos. 21, 4, 7, 11, 5, 8, and 6. III) Amines $(\text{R}_2\text{CH})_{0-2}\text{NH}_{3-1}$; expt. nos. 21, 9, 14, and 10. IV) Amines $(\text{R}_3\text{C})_{0-2}\text{NH}_{3-1}$; expt. nos. 21, 12, 13, and 31. V) Methylamines $(\text{CH}_3)_{2,3}\text{NH}_{1,0}$ (without catalyst); expt. nos. 46 and 47. VI) Ethanolamines $(\text{C}_2\text{H}_4\text{OH})_{2,3}\text{NH}_{1,0}$ (without catalyst); expt. nos. 49 and 50.

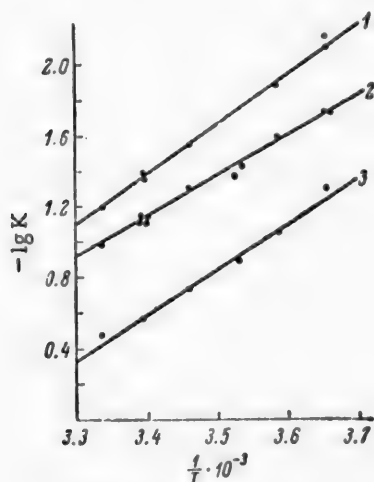


Fig. 3. Dependence of the rate constants for the oxidation of cyclohexylamine (1), triethylamine (2), and di-n-propylamine (3) on the temperature.

pertungstate, it is possible to conclude that the reaction goes because of the unshared pair of electrons, with the initial formation of a product of the amine-oxide type. In the case of ammonia and primary and secondary amines, the amine oxide (or amine-oxide hydrate) that is formed isomerizes to the corresponding hydroxylamine (Botvinnik [6]).

Effect of some functional groups in the amine molecule on the oxidation rate. For all practical purposes, the carbonyl and the ureido group, linked directly to the amino group, suppress oxidation completely. The

toward the peroxide oxygen is apparently determined by the number of hydrogen atoms attached to the nitrogen atom. The greater the number of hydrogen atoms, the slower the reaction rate (ammonia oxidizes the slowest of all). Molecules in which the number of N-H linkages is reduced (for example, amines, hydroxylamines, hydrazines, nitrite ion) are oxidized much more rapidly than ammonia. Tertiary amines (N-H linkages are absent) show the greatest affinity toward peroxide oxygen, which can be seen from a comparison of the activation energies for the oxidation of a number of amines: $\text{RNH}_2 = 13$, $\text{R}_2\text{NH} = 12$, and $\text{R}_3\text{N} = 10.5$ kcal/mole (Fig. 3), and also from the increase in the rate constant when amines in the $\text{R}_2\text{NH}-\text{R}_3\text{N}$ series are oxidized with hydrogen peroxide (Fig. 2, Curves V and VI). However, steric difficulties, which appear when the number of substituents is great, stand out prominently when tertiary amines are oxidized with pertungstate. Besides this, steric difficulties are associated with a branching of the substituent, since, in the series CH_3 , CH_2R , CHR_2 , and CR_3 the oxidation rate of the primary (RNH_2), secondary (R_2NH), and tertiary (R_3N) amines decreases (Fig. 2, comparison based on the verticals). The other oxidizing agent, namely permolybdate, oxidizes at a much slower rate, but it behaves in the same manner as the pertungstate when the discussion relates to the structure of the amines (Table 2).

The oxidation of aliphatic amines leads to the formation of compounds having oxygen attached to the nitrogen: amine oxides, hydroxylamines, and oximes. Thus, ammonia is oxidized to hydroxylamine, cyclohexylamine to cyclohexylhydroxylamine [2], and cyclohexanone oxime [1], diethylamine, and piperidine (using hydrogen peroxide without the sodium tungstate) to disubstituted hydroxylamines [3] and trimethyl- and triethylamines to the hydrates of the amine oxides [3,4]. Secondary amines, when oxidized with pertungstate, can oxidize to the oxime and carbonyl compound by rupture of the C-N single bond [5]. Ammonium ions, failing to have a free pair of electrons, do not oxidize. When it is considered that such different compounds as $\text{N}(\text{CH}_3)_3$, NH_3 , and NO_2^- , having only one common property, namely a nitrogen atom with an unshared pair of electrons, are oxidized by

amino acids also show very little oxidation, but when the carboxyl group is neutralized by alkali the amino group reacts readily. The oxidation rate increases when either a hydroxyl group or an amino group is found in the β -position to the nitrogen (ethanolamines, ethylenediamine). Heterocyclic amines (piperidine, hexamethylenimine, morpholine) also show a more rapid oxidation rate.

EXPERIMENTAL

The amines used in the work were either purchased, some of them being of Kahlbaum quality, or specially synthesized. A number of the commercial products were first purified. The oxidation rate of the amino compounds were measured using the following conditions: To 1.7 mmole of amino compound were added 0.5 mmole of NaOH, 1 mg of trilon B, 0.041 mmole of sodium tungstate, 3.4 mmole of hydrogen peroxide, and water to a total volume of 10.0 ml. The temperature was $21 \pm 0.5^\circ$.

For the amines insoluble in water, the reaction was run in the same volume, in the presence of 6.7-7.8 ml of ethanol. The experiment consisted in measuring the concentration of the amine being oxidized by titration with 0.1 N sulfuric acid, using phenolphthalein, and in the case of weakly basic amines, using bromocresol purple. A small change in the hydrogen peroxide concentration (1.7 to 3.4 mmole) fails to affect the reaction rate, but at a higher concentration (10 mmole) the oxidation rate decreases.

For most of the amines, we estimated the error in the values of the constants as being on the order of $\pm 20\%$ relative.

Oxidation of ammonia. When a mixture of 3.4 mmole of ammonia, 6.8 mmole of hydrogen peroxide, 3 mg of trilon B, and 0.32 mmole of sodium tungstate in a volume of 1.7 ml was allowed to react for 15 min, the amount of ammonia oxidized was 0.37 mmole, and the same amount was combined with the acids (NO_2^- and NO_3^-) formed. In the presence of 1.8 mmole of acetone, the amount of ammonia oxidized under the same conditions was 0.35 mmole (the amount of acetone oxime formed was 0.25 mmole). In the presence of cyclohexanone (the ammonia has to be taken in a larger amount, 7 mmole), some crystals separated after 20-60 min, which, after recrystallization from petroleum ether, had m.p. $87-88^\circ$ (according to [7], m.p. 90°). These crystals give the color test for the oxime group. The yield of cyclohexanone oxime was as high as 85%, based on the ketone.

The oxidation of cyclohexylamine was run using the conditions given in the patent [2]; a mixture composed of 100 g of the amine, 1.5 g of trilon B, 450 g of water, 110 ml of 30% hydrogen peroxide, and 6 g of sodium tungstate was stirred at 0° for 4 hr. The yield of cyclohexylhydroxylamine (m.p. $137-139^\circ$, literature m.p. 141°) did not exceed 40%, because of further oxidation to cyclohexanone oxime.

The oxidation of dicyclohexylamine was run under conditions different from those given in the patent [5]; a mixture composed of 8.5 mmole of the amine, 6.7 ml of ethanol, 1.5 ml of water, 2 mg of trilon B, 25 mmole of hydrogen peroxide, and 0.36 mmole of sodium tungstate was kept at $25-30^\circ$ for 6 hr. After making alkaline, the solution was extracted with ether to remove the cyclohexanone (oxime, m.p. $85-87^\circ$). After neutralization, the residual solution was extracted to remove the cyclohexanone oxime (m.p. $85-87^\circ$), which gives a positive color test for the oxime group.

Oxidation of trimethylamine. To a solution of 11 mmole of trimethylamine in 4 ml of ethanol were added 11 mmole of hydrogen peroxide, 3 mg of trilon B, 20 ml of water, and 0.6 mmole of sodium tungstate. The reaction went violently and intensive cooling was required. The reaction was ended in 10-15 min, the water was evaporated, the tungstate was salted out with alcohol, and the latter was also evaporated. We obtained 6.0 g of trimethylamine oxide hydrate, m.p. $95-96^\circ$ (from [4]: 96°). Yield 98%.

Oxidation of other compounds. 5 mmole of sodium nitrite is oxidized 50% (to nitrate) under the following conditions: volume of aqueous solution 4 ml, temperature 15° , sodium tungstate 0.16 mmole, trilon B 1 mg, NaOH 0.4 mmole, hydrogen peroxide 3.4 mmole. Urea, guanidine, and ϵ -caprolactam in the presence of alkali, and also cyclohexylamine hydrochloride and the amino acids in the absence of alkali (here it is necessary to take tungstic acid instead of sodium tungstate), fail to oxidize, since the amount of hydrogen peroxide did not change in several hours.

The following compounds are formed in the oxidation of all of the primary and secondary amines given in the table: oximes $\text{R}_2\text{C} = \text{NOH}$, hydroxylamines RNHOH , or hydroxamic acids RC(O)NROH . The oximes give a

yellow-red color with iron (III) solution, formalin, and hydrogen peroxide [1]. The substituted hydroxylamines give a red-violet color with the same solution, while the substituted hydroxamic acids give a red color with iron (III) ion alone, omitting the formalin and hydrogen peroxide [3].

SUMMARY

1. Aliphatic amines and ammonia are oxidized by hydrogen peroxide in the presence of sodium tungstate with the initial formation of a product of the amine oxide type, representing the addition of oxygen to the amine.
2. The rate constant for the oxidation of the amine depends on the number of hydrogen atoms attached to the nitrogen atom of the amine and on the number and degree of branching of the hydrocarbon substituents.

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CYCLOALKYLATION OF PHENOLS AND THEIR ETHERS

IV. CONDENSATION OF 1,1- AND 1,2-METHYLCYCLOHEXANOLS WITH PHENOL

A. R. Abdurasuleva and N. G. Koral'nik

Central Asian State University

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Continuing our study on the alkylation of phenols with cyclic alcohols, we investigated the reaction of phenol with 1,1- and 1,2-methylcyclohexanols in the presence of $AlCl_3$ or H_3PO_4 .

The condensation of phenol with either 1,1- or 1,2-methylcyclohexene in the presence of either concentrated sulfuric or acetic acid gave the same product, 4-(1-methylcyclohexyl)phenol [1]. The same compound was obtained [2] when phenol was reacted with 1,4-methylcyclohexanol in the presence of sulfuric acid. The formation of only the 4-(1-alkylcyclopentyl)phenol also occurred when phenol was reacted with various alkylcyclopentanols [3] in the presence of aluminum chloride. When phenol is alkylated with methylcyclopentyl chlorides [4], the same as when the methylcyclohexenes and methylcyclohexanols are used, the reaction products fail to contain any ethers, and only cycloalkylation of the ring occurs. However, when Sidorova [5] condensed phenol with 1,1-methylcyclohexanol in the presence of phosphoric acid, she obtained, in addition to 4-(1-methylcyclohexyl)phenol, also methylcyclohexyl phenyl ether, which could not be isolated in the pure form, since, on distillation, it isomerized completely to 4-(1-methylcyclohexyl)phenol.

*Original Russian pagination. See C.B. translation.

Para-orientation was also observed in the alkylation of β -naphthol with cyclohexanol and with its 2-, 3-, and 4-methyl and the ethyl homologs in the presence of phosphoric acid [6]. The same product was obtained when isomeric alcohols were used. However, the formation of unisomerized normal products [7] (although the melting points of the individual isomers are so close that the formation of the normal products becomes doubtful) was observed when phenol was condensed with the isomeric methylcyclohexanols in the presence of ZnCl_2 .

In our paper [8] on the alkylation of phenol with menthol we observed the formation, in addition to the isomerized optically inactive menthylphenol, of also optically active menthylphenol. This gives a basis also to expect, in the present case, a direct replacement of the hydroxyl of the alcohol without any isomerization.

The condensation of phenol with either 1,1- or 1,2-methylcyclohexanol in the presence of either phosphoric acid or aluminum chloride was run by us at different temperatures (20-150°). The proportions and order of adding the reagents was kept constant for each catalyst. The experiments with phosphoric acid were run employing the same conditions as in the experiments with cyclohexanol [9]. With aluminum chloride the reaction was run using equimolar proportions of alcohol and AlCl_3 and an 8-fold excess of phenol. Heating the reaction mixture on the boiling water bath for 5 hr appears to be the optimum condition for running these reactions in the presence of AlCl_3 or H_3PO_4 . Independent of the nature of the alcohol, catalyst, or temperature, the principal reaction product is 4-(1-methylcyclohexyl)phenol. The maximum yield with 1,1-methylcyclohexanol in the presence of either AlCl_3 or H_3PO_4 is 80%, while in the case of the 1,2-isomer it is 72-74%. The absence of normal reaction products in the case of 1,2-methylcyclohexanol again confirms the ease with which the alcohol radical is isomerized in the alkylation of phenols. Neither the ortho-isomer nor methylcyclohexyl phenyl ether could be detected in the reaction products.

EXPERIMENTAL

1,1-Methylcyclohexanol was obtained from cyclohexanone, b.p. 153-155° (730 mm). 1,2-Methylcyclohexanol was obtained by the reduction of o-cresol, b.p. 162-164° (730 mm).

Condensation of 1,1- and 1,2-methylcyclohexanols with phenol in the presence of AlCl_3 . Aluminum chloride was added over a period of 1.5-2 hr to the mixture of phenol and alcohol at room temperature. The AlCl_3 dissolved with the evolution of heat and some HCl evolution. Then the reaction mixture was allowed to stand at 20° (for 1 to 12 days), or else it was immediately heated (50-130°) for 5 hr. The reaction products were isolated either by vacuum distillation or by treatment with 20% caustic solution. Here only 4-(1-methylcyclohexyl)phenol with m.p. 109-111° was obtained.

When a mixture of 50 g of phenol, 7.4 g of 1,1-methylcyclohexanol, and 8.8 g of AlCl_3 was heated on the boiling water bath for 5 hr (with constant stirring) we obtained 10 g (80%) of 4-(1-methylcyclohexyl)phenol with b.p. 155-157° at 10 mm, and m.p. 110-111°.

When the reaction was run with 1,2-methylcyclohexanol under analogous conditions we obtained 9.2 g (74%) of 4-(1-methylcyclohexyl)phenol with b.p. 139-140° at 3 mm, and m.p. 110-111°.

Condensation of 1,1- and 1,2-methylcyclohexanols with phenol in the presence of H_3PO_4 . Phosphoric acid (d 1.86) was added to the phenol. This resulted in the formation of the ester, a white crystalline compound, which dissolved when the temperature was raised to 45-50°. Then the 1,1- or the 1,2-methylcyclohexanol was added from a dropping funnel, with constant stirring, in 1.5 hr. The reaction mixture was either allowed to stand at 20° or it was heated at 50-130° for 5 hr. The mixture gradually changed in color from a yellow to a bright crimson. The mixture separated into layers on cooling. The next day the upper layer turned crystalline, while the lower layer remained liquid. The further workup and isolation of the reaction products were the same as in the experiment with AlCl_3 .

1,1-Methylcyclohexanol (7.4 g) was added from a dropping funnel to a mixture of phenol (8 g) and H_3PO_4 (30 g) on the boiling water bath. Then the mixture was heated at the same temperature for another 5 hr. We obtained 9 g (72%) of 4-(1-methylcyclohexyl)phenol with b.p. 150-153° at 8 mm, and m.p. 110-111°. With 1,2-methylcyclohexanol under the same conditions we obtained 10 g (80%) of 4-(1-methylcyclohexyl)phenol with b.p. 150-152° at 7 mm, and m.p. 108-110°.

Identification of 4-(1-methylcyclohexyl)phenol. The products obtained using the same condensation catalyst were combined and recrystallized again. M.p. 112° (from petroleum ether). From the literature [1], m.p.

112.5°. The benzyl ether with m.p. 82-83°, and the nitrobenzyl ether with m.p. 153-154° [5] were prepared. The methylether had m.p. 41° [2], b.p. 130-132° at 8 mm, n_D^{20} 1.5343, d_4^{20} 1.005, M_R^D 63.1, calc. 62.9.

Oxidation of the methyl ether with nitric acid (d 1.1) gave p-methoxybenzoic acid with m.p. 183°.

2,6-Dinitro-4-(1-methylcyclohexyl)phenol was obtained by the earlier-described method [9] in glacial acetic acid solution, by reacting the phenol with nitric acid (d 1.4) at 15-20°. Bright-yellow crystals with m.p. 72-73°.

Found %: N 9.88. $C_{15}H_{16}O_5N_2$. Calculated %: N 9.99.

4-(1-Methylcyclohexyl)phenoxyacetic acid was obtained in conventional manner [10]. M.p. 104-105° (from petroleum ether).

Found %: C 72.22; H 8.65. $C_{15}H_{20}O_3$. Calculated %: C 72.14; H 8.60.

SUMMARY

1. Independent of the catalyst or temperature used, the condensation of either 1,1-methyl- or 1,2-methylcyclohexanol with phenol always yields only 4-(1-methylcyclohexyl)phenol.

2. The previously unknown 2,6-dinitro-4-(1-methylcyclohexyl)phenol and 4-(1-methylcyclohexyl)phenoxyacetic acid were synthesized.

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*Original Russian pagination. See C.B. translation.

STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XX. SYNTHESIS OF ESTERS OF SECONDARY α -HYDROXY ACIDS OF THE ALIPHATIC AND ALICYCLIC SERIES

I. I. Lapkin and N. A. Karavanov

Perm State University

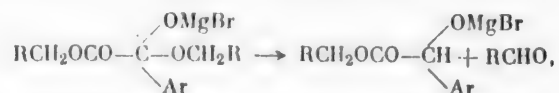
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Depending on the reaction conditions, the proportions of the reactants, the nature of the radicals of the organomagnesium compounds, and the structure of the alkoxy group present in the oxalic acid ester, the reaction of oxalic acid esters with organomagnesium compounds leads to the formation of extremely diverse products. By varying these factors it becomes possible to stop the reaction at one of the intermediate stages and, in this way, obtain homogeneous products.

Thus, it was established earlier [1-6] that varying only two factors, namely increasing the complexity of the aryl radicals contained in the organomagnesium compounds, or of the alkoxy groups present in the oxalic acid esters, which naturally leads to an increase in the steric hindrance, and changing the order of mixing the reactants (the organomagnesium compound was added to the ester) makes it possible to stop the reaction at the first stage. The complex formed in the first stage of the reaction is not stable, and decomposes even at the boiling point of the ether solution (40-42°), in accordance with the equation [3]:



which leads after hydrolysis to the formation of esters of secondary α -hydroxy acids.

The purpose of the present investigation was to use this method in the synthesis of both aliphatic and alicyclic esters belonging to this class of compounds.

The complex is more stable when the aryl radicals are replaced by alkyls and no longer decomposes at the boiling point of the ether solution, consequently requiring a higher temperature (110-120°) for its decomposition. Complete decomposition of the complex is achieved by adding toluene to the reaction mixture, then distilling off the ether, and subsequently refluxing the toluene solution for 2 hr.

Complexes containing an alicyclic radical, in particular the cyclohexyl group, decompose with the same ease as the complexes containing an aryl radical, even at the boiling point of the ether solution, i.e., under the normal conditions of organomagnesium reactions.

The results of our investigation are summarized in the table.

EXPERIMENTAL

The general conditions used to react oxalic acid esters with organomagnesium compounds for the purpose of obtaining esters of secondary α -hydroxy acids of the aliphatic series are as follows.

The ether solution of organomagnesium compound (0.25 mole) was added to a solution of the oxalic acid ester (0.25 mole) in 2 volumes of anhydrous diethyl ether, cooled in an ice-salt mixture. Then toluene, taken in approximately the same volume as the first solvent, was added to the reaction mixture, the diethyl ether was distilled off, and the toluene solution was refluxed for 2 hr. After this, the reaction mixture, as is customary, was hydrolyzed with water and 10% hydrochloric acid, and the toluene layer was washed with 10% sodium bicarbonate solution and then with sodium sulfate solution to break the emulsion. The addition of hydrochloric

Reactants (1:1)	Yield of ester (%)	Name of ester*	Boiling point (pressure in mm)	Melting point	Empirical formula	Amount (in %)						n _D	d ₄	M _r R ₂			
						C		H		OH				found	calc.	found	calc.
						found	calc.	found	calc.	found	calc.						
n-Butylmagnesium bromide + diethyl oxalate	35	Ethyl α-hydroxy- caproate	67—68 (3)	—	C ₈ H ₁₆ O ₃	59.78	59.96	9.94	10.06	10.1	10.6	1.4240 (23°)	0.9659 (23°)	42.32	42.32		
n-Heptylmagnesium bromide + di-n- propyl oxalate	52	n-Propyl α-hy- droxypelargonate	126 (8)	—	C ₁₂ H ₂₄ O ₃	66.43	66.62	11.11	11.19	7.2	7.9	1.4378 (19°)	0.9298 (19°)	60.96	60.80		
n-Heptylmagnesium bromide + diiso- propyl oxalate	40	Isopropyl α- hydroxy- pelargonate	106 (4)	—	C ₁₂ H ₂₄ O ₃	66.45	66.62	11.05	11.19	7.3	7.9	1.4330 (21°)	0.9206 (21°)	60.97	60.80		
n-Heptylmagnesium bromide + di-n- butyl oxalate	50	n-Butyl α-hy- droxypelargo- nate	125 (5)	—	C ₁₃ H ₂₆ O ₃	67.70	67.78	11.28	11.37	7.1	7.4	1.4390 (20°)	0.9223 (20°)	65.59	65.41		
n-Heptylmagnesium bromide + diiso- butyl oxalate	46	Isobutyl α- hydroxy- pelargonate	120 (5)	—	C ₁₃ H ₂₆ O ₃	67.61	67.78	11.25	11.37	7.0	7.4	1.4376 (19°)	0.9198 (19°)	65.59	65.41		
n-Octylmagnesium bromide + di-n- propyl oxalate	49	n-Propyl α- hydroxy- caprate	107—108 (3)	23	C ₁₃ H ₂₆ O ₃	67.58	67.78	11.24	11.37	6.9	7.4	—	—	—	—		

* All of the synthesized compounds, with the exception of ethyl α-hydroxyundecanoate, for which a m.p. of 33° is given in the literature [8], are new.

(continued)

Reactants (1:1)	Yield of ester (%)	Name of ester	Boiling point (pressure in mm)	Melting point	Empirical formula	Amount (in %)						n _D	d ₄	MR _D	
						C		H		OH					
						found	calc.	found	calc.	found	calc.			found	calc.
n-Octylmagnesium bromide + diiso- propyl oxalate	40	Isopropyl α- -hydroxy- caprate	102—104 (3)	25	C ₁₃ H ₂₆ O ₃	67.65	67.78	11.27	11.37	7.2	7.4	—	—	—	—
n-Octylmagnesium bromide + di-n- butyl oxalate	42	n-Butyl α- -hydroxy- caprate	109—110 (2)	21	C ₁₄ H ₂₈ O ₃	68.63	68.81	11.45	11.55	6.5	7.0	—	—	—	—
n-Octylmagnesium bromide + diiso- butyl oxalate	41	Isobutyl α- -hydroxy- caprate	105—107 (2)	22	C ₁₄ H ₂₈ O ₃	68.61	68.81	11.38	11.55	6.6	7.0	—	—	—	—
n-Nonylmagnesium bromide + diethyl oxalate	48	Ethyl α- hydroxy- undecanoate	113—115 (3)	34	C ₁₃ H ₂₆ O ₃	67.60	67.78	11.28	11.37	7.1	7.4	—	—	—	—
n-Nonylmagnesium bromide + di-n- propyl oxalate	51	n-Propyl α- -hydroxy- undecanoate	122—123 (4)	22	C ₁₄ H ₂₈ O ₃	68.60	68.81	11.46	11.55	6.7	7.0	—	—	—	—
n-Nonylmagnesium bromide + diiso- propyl oxalate	50	Isopropyl α- -hydroxy- undecanoate	122—124 (5)	24	C ₁₄ H ₂₈ O ₃	68.65	68.81	11.42	11.55	6.5	7.0	—	—	—	—
n-Nonylmagnesium bromide + di-n- butyl oxalate	48	n-Butyl α- -hydroxy- undecanoate	130—131 (4)	22	C ₁₅ H ₃₀ O ₃	69.54	69.72	11.60	11.70	6.0	6.6	—	—	—	—

Reactants (1:1)	Yield of ester (%)	Name of ester	Boiling point (pressure in mm)	Melting point	Empirical formula	Amount (in %)						n _D	d ₄	M _R		
						C		H		OH						
						found	calc.	found	calc.	found	calc.			found	calc.	
n-Nonylmagnesium bromide + diisobutyl oxalate	50	Isobutyl α- -hydroxy- undecanoate	125—127 (4)	23	C ₁₅ H ₃₀ O ₃	69.55	69.72	11.61	11.70	6.2	6.6	—	—	—	—	
Cyclohexylmagnesium chloride + diethyl oxalate	42	Ethyl cyclo- hexylglycolate	89 (3)	—	C ₁₀ H ₁₈ O ₃	64.30	64.48	9.63	9.74	8.8	9.1	1.4530 (23°)	—	1.0335 (23°)	49.20	49.34
Cyclohexylmagnesium chloride + di-n- propyl oxalate	44	n-Propyl cyclo- hexylglycolate	102—103 (4)	—	C ₁₁ H ₂₀ O ₃	65.78	65.97	9.96	10.07	8.0	8.5	1.4608 (17°)	—	1.0049 (17°)	54.59	53.93
Cyclohexylmagnesium chloride + diisopropyl oxalate	40	Isopropyl cyclo- hexylglycolate	98—100 (4)	—	C ₁₁ H ₂₀ O ₃	65.82	65.97	9.95	10.07	8.1	8.5	1.4582 (20.5°)	—	1.0188 (20.5°)	53.66	53.93
Cyclohexylmagnesium chloride + di-n-butyl oxalate	45	n-Butyl cyclo- hexylglycolate	112—113 (2.5)	—	C ₁₂ H ₂₂ O ₃	67.08	67.25	10.27	10.35	7.6	8.0	1.4621 (19.5°)	—	1.0063 (19.5°)	58.48	58.57
Cyclohexylmagnesium chloride + diisobutyl oxalate	40	Isobutyl cyclo- hexylglycolate	110 (3)	—	C ₁₂ H ₂₂ O ₃	67.05	67.25	10.25	10.35	7.7	8.0	1.4620 (19°)	—	1.0107 (19°)	58.21	58.57

acid to the used sodium bicarbonate solution usually gave a small amount (about 2 g) of α -hydroxy acid, formed by the saponification of the α -hydroxy acid ester.

The toluene solution was dried over anhydrous sodium sulfate, the solvent was distilled off, and the product remaining in the flask was vacuum distilled.

If the boiling point of the reaction product (for example ethyl *n*-butylglycolate), was close to that of the oxalic acid ester then, to remove the latter, the product was subjected to a more precise fractionation. Its properties were verified in such cases by saponification of the ester, followed by resynthesis of the ester from the obtained hydroxy acid. For this a solution of the α -hydroxy acid in excess alcohol was saturated in the cold with hydrogen chloride, the reaction mixture then poured into water, and the ester of the hydroxy acid extracted with diethyl ether.

The properties of the esters obtained in this manner always proved to be very close to the properties of the esters that were synthesized by direct reaction of the organomagnesium compounds with the oxalic acid esters, which testifies to the purity of the synthesized products.

A certain amount of the ester of the tertiary hydroxy acid was also obtained in the synthesis of the low-molecular esters of the hydroxy acids (when $n\text{-C}_4\text{H}_9\text{MgBr}$ or $\text{iso-C}_5\text{H}_{11}\text{MgBr}$ was taken as the organomagnesium compound).

The complexes formed when mixed alicyclic organomagnesium compounds are reacted with oxalic acid esters prove to be unstable and decompose in accordance with the above-given equation even at the boiling point of the ether solution, for which reason the synthesis of the cyclohexylglycolic acid esters was run in ether solution without the addition of toluene.

The methyl ester of α -hydroxypelargonic acid, not listed in the table, was synthesized as indicated above by saturating a solution of the acid in excess methyl alcohol with hydrogen chloride in the cold. The compound is new.

B.p. 108° at 6 mm, d_4^{20} 0.9564, n_D^{20} 1.4375, M_R^D 51.56; calc. 51.56.

Found %: C 63.65; H 10.65; OH 8.7. $\text{C}_{10}\text{H}_{20}\text{O}_3$. Calculated %: C 63.79; H 10.70; OH 9.0.

The reaction between isoamylmagnesium bromide and di-*n*-butyl oxalate, the result of which is also not given in the table, was run under the above-described conditions, except that the obtained ester, without investigating it further, was saponified with alcoholic caustic solution. The yield of 2-methyl-5-hydroxy-6-hexanoic acid was 35%. M.p. $61\text{--}62^\circ$ (from petroleum ether). From [7]: m.p. 60.5° .

SUMMARY

1. A method was developed for the synthesis of esters of secondary α -hydroxy acids of the aliphatic and alicyclic series, based on reacting oxalic acid esters with organomagnesium compounds, and subsequently refluxing the formed complex in toluene solution (esters of aliphatic hydroxy acids) or in ether solution (esters of alicyclic hydroxy acids). The complex $[\text{RCH}_2\text{OCO}-\text{C}(\text{OMgBr})(\text{OCH}_2\text{R})\text{R}']$ decomposes under these conditions with the formation of either aldehyde (RCHO) or ketone, the latter in the case of a secondary radical, and the bromomagnesium alcoholate of the hydroxy acid ester $[\text{RCH}_2\text{OCO}-\text{CH}(\text{OMgBr})\text{R}']$.

2. Nineteen new esters of α -hydroxy acids were synthesized.

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THE PREPARATION OF n-AMYL ALCOHOL FROM TRIOXYMETHYLENE AND n-BUTYLMAGNESIUM BROMIDE

G. V. Medoks and L. E. Ozerskaya

Saratov Agricultural Institute

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The preparation of n-amyl alcohol by the reaction of trioxymethylene (paraformaldehyde) with n-butylmagnesium bromide was first reported by Bourgoin [1]. The same reaction was studied later by Levaillant [2], who isolated both n-amyl alcohol and di-n-amyl formal from the obtained products. However, neither author gave any information as to the experimental conditions or the yield of n-amyl alcohol. In 1938 [3], the synthesis of n-amyl alcohol was described in detail, and here it was obtained in 68% yield from n-butylmagnesium bromide and trioxymethylene, in which connection the latter reactant was first converted by heating to formaldehyde and only then introduced into reaction. After distilling off the ether, the mentioned American investigators washed the mixture of the reaction products with sodium bisulfite solution, apparently to remove the unreacted formaldehyde. However, as our experiments revealed, it is more expedient to remove the formaldehyde or trioxymethylene before distilling off the ether since they, reacting easily with n-amyl alcohol, give di-n-amyl formal, which not only lowers the yield of synthesized alcohol, but also complicates its further isolation in the pure state. Taking these facts into consideration, we reacted trioxymethylene with n-butylmagnesium bromide using a 9.6% excess of the latter when compared to the stoichiometric amount, and obtained n-amyl alcohol in 92.3% yield, based on the taken trioxymethylene.

EXPERIMENTAL

To the Grignard reagent, prepared from 97 g of n-butyl bromide dried over phosphorus pentoxide, 17.2 g of magnesium, and 205 ml of absolute ether, and transferred to a flask protected by a calcium chloride tube, was added 16.7 g of finely powdered trioxymethylene, previously dried in a desiccator over calcium chloride. The yield of mixed organomagnesium compound was 86.0% of theory. Within 5 min after starting to shake the liquid with the solid a strong evolution of heat was observed, and it became necessary to cool the mixture with cold water. Then the reaction mixture was allowed to stand at 25-26° for 5 days, with periodic shaking. At the end of this time the mixture of solid reaction products was cooled in ice water and decomposed gradually by the addition of 130 ml of 10% hydrochloric acid. We collected 625 ml of butane over water at 28° and 763 mm. The ether layer was separated from the water layer and the latter, containing a small deposit of unreacted trioxymethylene, was extracted 6 times with ether (300 ml). The ether extracts were added to the main ether layer, after which the whole was shaken well with 50 ml of saturated sodium bisulfite, and then the mixture was allowed to stand for two days with periodic shaking, until the test for formaldehyde using fuchsin-sulfite reagent was negative. The filtered liquid was then dried over potassium carbonate, the ether was distilled on the water bath, and the oily residue (57.0 g) was fractionally distilled to give 8.0 g of a fraction with b.p. 73-126°, being a mixture of n-octane, n-butyl alcohol, n-butyl bromide, and the ether, 45.2 g of main fraction with b.p. 137.6-138.2°, which proved to be n-amyl alcohol (d_{4}^{20} 0.814), and 1.0 g of residue, which was free of di-n-amyl formal.

An experiment run under analogous conditions, but without a careful removal of the unreacted trioxymethylene, and using only a 6.2% excess of n-butylmagnesium bromide, resulted in obtaining a product that required

*Original Russian pagination. See C.B. translation.

repeated fractionation to free the obtained *n*-amyl alcohol (73% yield) from (mainly) di-*n*-amyl formal, always formed along with water from the amyl alcohol and trioxymethylene during distillation.

SUMMARY

Conditions were developed for obtaining *n*-amyl alcohol from trioxymethylene and *n*-butylmagnesium bromide in 92.3% of the theoretical yield.

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SYNTHESIS OF BIS-1,3,4-OXADIAZOLE DERIVATIVES

A. P. Grekov and M. S. Solov'eva

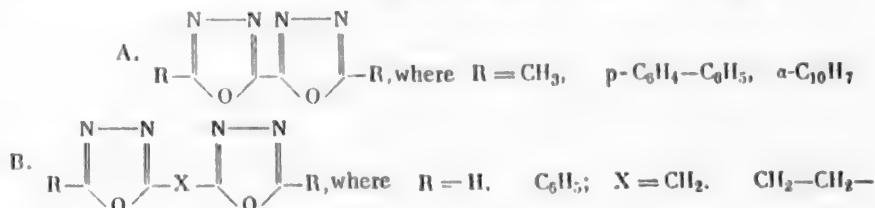
Khar'kov Branch of the Institute of Reagents

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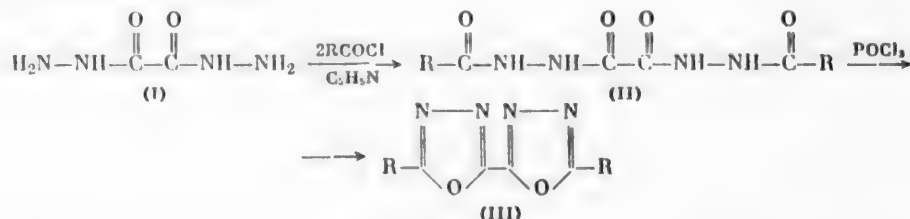
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Bis-1,3,4-oxadiazole derivatives have received very little study up to now. In order to study their properties, it seemed expedient to synthesize a number of new compounds of the type of A and B:



To obtain compounds of the A type, where R is either an aliphatic or an aromatic radical, we resorted to the method usually used to synthesize highly different 2,5-derivatives of 1,3,4-oxadiazole [1], which, in our case, can be depicted by the following scheme:



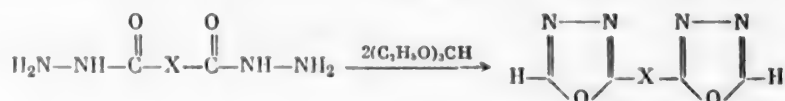
With this same scheme we also obtained bis-1,3,4-oxadiazole derivatives of the B type, where the oxadiazole rings are separated by a hydrocarbon chain, and here we had to use the hydrazide of the appropriate acid,

In the process of synthesizing the secondary dihydrazide (II) from the primary dihydrazide (I) and appropriate acid chloride in pyridine medium, we found that, for a number of the compounds, together with the main reaction product, a substantial amount of a substance was obtained that from its properties and analysis results corresponded to the diacylhydrazine which, on treatment with POCl₃, gave the corresponding 2,5-derivative of 1,3,4-oxadiazole.

Compound	Melting point (solvent)	Yield (%)	Formula	% N	
				found	calc.
5,5'-Dimethyl-2,2'-bis- -1,3,4-oxadiazolyl	217,5° (from alcohol)	14	C ₆ H ₆ O ₂ N ₄	33.70	33.73
5,5'-Di-(4-diphenyl)-2,2'- -bis-1,3,4-oxadiazolyl	325° (from dioxane)	99	C ₂₈ H ₁₈ O ₂ N ₄	12.56	12.66
5,5'-Di-(1-naphthyl)-2,2'- -bis-1,3,4-oxadiazolyl	295° (from dioxane and toluene)	99	C ₂₄ H ₁₄ O ₂ N ₄	14.40	14.35
1,2-Di-[2-(1,3,4-oxadiazolyl)]-ethane	152° (from benzene and toluene)	57	C ₆ H ₆ O ₂ N ₄	33.67	33.70
1,2-Di[2-(5-phenyl-1,3,4- -oxadiazolyl)]-ethane	141,5° (from alcohol)	75	C ₁₈ H ₁₄ O ₂ N ₄	17.86	17.61
1,1'-Di-[2-(1,3,4-oxadiazolyl)]-2-ethoxyethane	157° (from alcohol)	39	C ₈ H ₈ O ₃ N ₄	26.85	26.90

In the case of synthesizing the bis-1,3,4-oxadiazole derivatives where the two rings are separated by a methylene bridge, we were unable to obtain satisfactory results, since the hydrogens of the CH₂ group reacted readily with the reagents used.

To obtain the bis-1,3,4-oxadiazole derivatives where R = H, we reacted ethyl orthoformate with the primary dihydrazide of the acid [2] in accordance with the following equation:



However, we were unable to obtain the bis-1,3,4-oxadiazole from oxalic acid hydrazide and ethyl orthoformate using this method, since complex reaction products were obtained as the reaction result here, and we failed to take time out to determine their structure. The reaction of ethyl orthoformate with malonic acid hydrazide gave us the bis-1,3,4-oxadiazole derivative where the hydrogens of the methylene group were replaced by the =CH-OC₂H₅ group.

The bis-1,3,4-oxadiazole derivatives obtained in the present study are colorless crystalline compounds, readily hydrolyzed by aqueous solutions of acids and alkalis with the formation of the starting dihydrazides. The bis-1,3,4-oxadiazole derivatives, where R = H or CH₃, are hydrolyzed with unusual ease. All of the bis-1,3,4-oxadiazole derivatives synthesized by us were purified by recrystallization from suitable solvent until the melting point remained constant, and then they were subjected to elemental analysis. In some cases, the structure of the compounds was confirmed by counter synthesis.

EXPERIMENTAL

Synthesis of 5,5'-di-(1-naphthoyl)-2,2'-bis-1,3,4-oxadiazole. a) Di-(1-naphthoyl)hydrazide of oxalic acid. To a solution of 20 g of 1-naphthoyl chloride in 100 ml of dry pyridine was slowly added 6.2 g of oxalic acid hydrazide [3], after which the flask contents were refluxed for 30 min and then poured into 500 ml of cold water. After 2-3 hr, the obtained deposit of white amorphous product was filtered, washed on the filter with water, then with alcohol, and dried. Yield 19.4 g (87%); the material chars above 300°.

b) 5,5'-Di-(1-naphthyl)-2,2'-bis-1,3,4-oxadiazolyl. A mixture of 10 g of oxalic acid di-(1-naphthoyl)-hydrazide and 500 ml of POCl₃ was heated under reflux for 15 hr, after which treatment nearly all of the precipitate went into solution. Then 350 ml of POCl₃ was removed by distillation, while the residue was poured over 500 g of ice (much heat was evolved). The obtained reaction product was filtered, washed on the filter with water, and dried. Yield 9.1 g (99%), m.p. 235°. Several recrystallizations from dioxane and from toluene gave 5,5'-di-(1-naphthyl)-2,2'-bis-1,3,4-oxadiazolyl with m.p. 294-295°.

Found %: N 14.40. C₂₄H₁₄O₂N₄. Calculated %: N 14.35.

Synthesis of 1,2-di-[2-(1,3,4-oxadiazolyl)]-ethane. A mixture of 15 g of succinic acid dihydrazide [3] and 850 ml of ethyl orthoformate was heated under reflux for 16 hr, and here all of the dihydrazide went into solution. Then most of the ethyl orthoformate was distilled off, and the residue on cooling deposited a crystalline product with m.p. 137-140°. Yield 9.7 g (57%). After several recrystallizations from benzene and from toluene the 1,2-di-[2-(1,3,4-oxadiazolyl)]-ethane was obtained with m.p. 151-152°.

Found %: N 33.67. $C_6H_6O_2N_4$. Calculated %: N 33.70.

The other bis-1,3,4-oxadiazole derivatives listed in the table were obtained employing similar procedures.

SUMMARY

Six new bis-1,3,4-oxadiazole derivatives of various structures were synthesized.

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COCONDENSATION OF DIARYLAMINES WITH ISOVALERALDEHYDE

V. I. Minkin, B. I. Ardashev, and K. A. Tskhadadze

Rostov-on-Don State University

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In previous papers [1,2] we described our modification of the Doebner-von Miller reaction [3] with secondary amines, based on running the main stages of the synthesis in two separate steps: formation of the bis-vinyl-diarylamine bases, and their conversion to the quinolium salt.

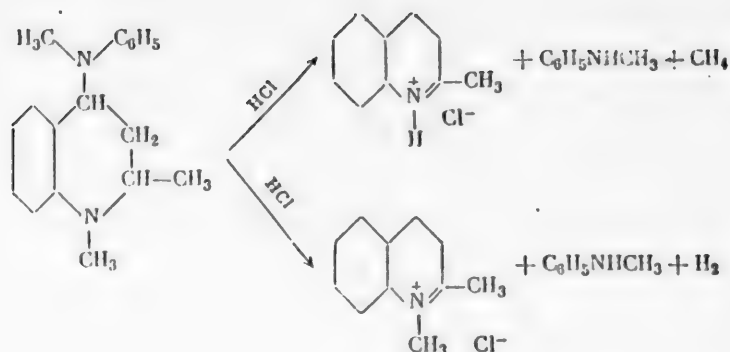
In contrast to the earlier-known methods [4-7], it was shown [2] that it is possible to use the higher aliphatic aldehydes, like propionaldehyde, butyraldehyde, etc. in the reaction.

In this paper we describe some new N-aryl-2,3-dialkylquinolium derivatives, obtained by the cocondensation of some secondary aromatic amines with isovaleraldehyde. We are of the opinion that the mechanism of the reaction is the same as that proposed earlier [1,2]. We assume that cyclization in the case of the unsymmetrical diarylamines goes with involvement of the more nucleophilic aryl group, as had been established by Pilyugin [4].

The Doebner-von Miller reaction with secondary amines was also extended to the secondary aliphatic aromatic amines. In the reaction with N-methylaniline we obtained a small yield of N-methylquinolium perchlorate, which is apparently explained by decomposition of the intermediate vinylmethylaniline dimer with the liberation of methane, the same as occurs in high-temperature distillation [8,9]. (See scheme on following page.)

As a result, the reaction as developed by us goes with various aromatic, aliphatic aromatic, and acylated primary [2] amines, and also with various aliphatic aldehydes, and is a general method for the synthesis of the arylates and alkylates of quinaldine and 2,3-dialkylquinolines.

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It was established that other polar solvents besides nitrobenzene can be used with success in the reaction, which was shown on the example of obtaining N-phenylquinolindinium perchlorate from diphenylamine and acet-aldehyde ethylal.

o-Nitrodiphenylamine, 2,4-dinitrodiphenylamine, and N-phenylanthranilic acid failed to form quinolinium salts, which is explained by the weak basicity of these amines. It is interesting that indole also fails to form the quinolinium salt.

EXPERIMENTAL

The reactions were run in a round-bottomed flask fitted with a reflux condenser.

1. N-phenyl-2-isobutyl-3-isopropylquinolinium perchlorate. A mixture of 5.0 g of diphenylamine, 9 ml of isovaleraldehyde, and 15 ml of nitrobenzene was heated under moderate reflux for 8 hr. Then 10 ml of hydro-chloric acid (d 1.18) was added, and the nitrobenzene and excess aldehyde were steam distilled. Here nearly all of the unreacted diphenylamine turned to a tar and coated the walls of the distillation flask. The solution was decolorized by boiling with activated carbon, followed by cautious evaporation to a volume of 30-50 ml. The difficultly soluble perchlorate was precipitated by the addition of perchloric acid to the residual solution. Yield 0.65 g (10.7% of theory, based on the mechanism assumed for the reaction [2]). M.p. 246° (from water). Fine yellow needles.

Found %: Cl 8.90, 8.73. $C_{22}H_{26}O_4NCl$. Calculated %: Cl 8.78.

2. N-Phenyl-2-isobutyl-3-isopropyl-5,6-benzoquinolinium perchlorate. A mixture of 6.5 g of N-phenyl-2-naphthylamine, 10 ml of isovaleraldehyde, and 20 ml of nitrobenzene was heated under moderate reflux for 8 hr. Then 10 ml of concentrated hydrochloric acid was added, and the nitrobenzene and unreacted aldehyde were steam distilled. After the usual treatment with perchloric acid we obtained 0.7 g of the perchlorate as flocculent, pale yellow crystals (11% yield). M.p. 174° (from water; with decomp.).

Found %: Cl 7.92, 7.94. $C_{26}H_{28}O_4NCl$. Calculated %: Cl 7.81.

3. N-Phenyl-2-isobutyl-3-isopropyl-6-methylquinolinium perchlorate. A mixture of 1.35 g of N-phenyl-p-tolylamine, 3 ml of isovaleraldehyde, and 8 ml of nitrobenzene was heated under moderate reflux for 6 hr. Then 5 ml of concentrated hydrochloric acid was added, and the nitrobenzene and excess aldehyde were steam-distilled. Subsequent treatment, as described in experiment 1, gave 0.16 g (10%) of the perchlorate as fine, light-pink needles. M.p. 227-228° (from water).

Found %: Cl 8.62, 8.70. $C_{23}H_{28}O_4NCl$. Calculated %: Cl 8.49.

4. N-p-Tolyl-2-isobutyl-3-isopropyl-6-methylquinolinium perchlorate. A mixture of 1.1 g of p,p'-di-tolylamine, 3 ml of isovaleraldehyde, and 8 ml of nitrobenzene was heated under moderate reflux for 6 hr. Then 5 ml of concentrated hydrochloric acid was added, and the nitrobenzene and excess aldehyde were steam distilled. Isolation in the same manner as described in experiment 1 gave 0.16 g of the perchlorate as fine yellow needles (13% yield). M.p. 229-231° (from aqueous ethanol; with decomp.).

Found %: Cl 8.35, 8.41. $C_{24}H_{30}O_4NCl$. Calculated %: Cl 8.21.

5. N-Phenylquinaldinium perchlorate. In order to determine the effect of the nature of the solvent on the yield of the N-arylquinolinium salts, we ran several experiments employing the following procedure.

A mixture of 1 g of the diphenylamine, 12 ml of acetaldehyde, 2 ml of nitrobenzene (oxidizing agent), and 20 ml of the solvent was heated for 6 hr. The technique used to run the experiments and isolate the phenylquinaldinium perchlorate was the same as that described earlier [1]. The melting points of the obtained perchlorates agreed with those given in the literature, while the mixed melting points with authentic N-phenylquinaldinium perchlorate were not depressed. The data on the change in yield as a function of the solvent used are given below.

Effect of Nature of Solvent on Yield of N-Phenylquinaldinium Perchlorates

Solvent	Yield based on diphenylamine (in %)
Nitrobenzene [1]	22
Chlorobenzene	20
Isoamyl alcohol	23
p-Xylene	13
Dioxane	16

6. N-Methylquinaldinium perchlorate. A solution of 10.6 g of freshly distilled N-methylaniline and 15 ml of paraldehyde in 50 ml of nitrobenzene was heated at 120° for 4 hr. Then the mixture was cooled, 40 ml of concentrated hydrochloric acid was added, and the nitrobenzene was slowly steam distilled.

The aqueous solution was filtered from tar, the residue in the flask was extracted with 50 ml of hot water, and then the combined water extracts were washed with benzene, followed by shaking with activated carbon. Then 4 g of sodium iodide was added to the filtrate, and the solution was cautiously evaporated to dryness on the water bath. This was followed by extraction of the residue with 25 ml of hot water, which was washed with chloroform and then decolorized with activated carbon. The filtrate was treated with 4 ml of concentrated perchloric acid (65%). Here the N-methylquinaldinium perchlorate precipitated. Yield 2.52 g (10%). M.p. 155°.

Found %: Cl 13.87, $C_{11}H_{12}O_4NCl$. Calculated %: Cl 13.76.

SUMMARY

1. The condensation of diarylamines with isovaleraldehyde gave some new N-aryl-2-isobutyl-3-isopropylquinolinium derivatives.
2. It was shown that the reaction as developed by us can be extended to the secondary aliphatic-aromatic amines.
3. The influence of the nature of the solvent on the yield of the N-arylquinolinium derivatives was examined.

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STUDY OF THE MECHANISM OF THE CONDENSATION OF AMINO COMPOUNDS, USING N¹⁵

B. A. Geller and L. S. Samosvat

L. I. Pisarzhevskii Institute of Physical Chemistry,
Academy of Sciences of the Ukrainian SSR

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The mechanism for the formation of N-phenyl- α -naphthylamine and benzarylides in the condensation of two amino compounds was investigated in the paper by Brodskii, Sheinfain, and one of us [1]. The scope of the investigated reactions was expanded in the present paper, and data were collected that not only permit supplementing the previous concepts regarding the mechanism, but also allow us to express some new theories.

We investigated the paths for the cleavage of the amino group in the condensation of p-aminophenol with aniline, α -naphthylamine, and benzamide, of n-butylamine with aniline, and of the p- and m-chloroanilines with α -naphthylamine. In all cases, the amino group in one of the components was enriched with heavy nitrogen. Then by determining the amount of heavy nitrogen in the products obtained by the reaction [the general scheme of the reaction is depicted by (1)] of secondary amine and ammonium chloride, it was possible to establish the place of cleavage of the amino group.



We will mention that analyzing the ammonium chloride in those cases where the investigated reaction is accompanied by a number of side processes, also taking place with the cleavage of ammonia, is meaningless. In such cases we analyzed only the secondary amine, isolated from the reaction mixture and then carefully purified, for the content of nitrogen isotopes.

The condensation was run in sealed ampoules. Only in the condensation of p-aminophenol with aniline was the reaction run at atmospheric pressure in a nitrogen stream. One of the amines was taken as the hydrochloride. The ampoules were heated in a thermostat for a predetermined length of time. The ammonium chloride was extracted by treating the reaction mixture with water. Then the secondary amine was isolated, purified, digested by the Kjeldahl method, and the nitrogen converted to ammonium chloride. Then the two samples of ammonium chloride were analyzed for their content of nitrogen isotopes.

The results of the mass-spectrometric analysis for nitrogen are shown in Table 1.

We have also given the basicities of the reacting amines in Table 1, characterized as the base dissociation constants K_b .

In most of the reactions the amino group is cleaved from only one of the components. If the order of cleavage of the amino group is compared with the basicities of the amines, then the following is revealed. In reaction 1, the amino group is cleaved from the weaker base - α -naphthylamine; in reactions 2 and 3 it is cleaved from the stronger base - p-aminophenol; in reaction 4, it is cleaved approximately two-thirds from the weaker α -naphthylamine and one-third from the stronger base - p-aminophenol; in reaction 6, it is cleaved from the stronger base - n-butylamine; in reaction 7, with the basicities the same, it is cleaved only from the α -naphthylamine; in reaction 8 it is cleaved from the stronger base - α -naphthylamine.

It is obvious that using only the basicities of the amines as a guide in elucidating the mechanism is out of the question. We postulate that the mechanism for the reaction of two amines may depend on those properties that are most different for a given pair of amines. For example, it can be seen from the data in Table 1 that α -naphthylamine always loses its amino group when it is condensed with an amine of the benzene series.

Re- action No.	Starting compounds					Atom % N ¹⁵ in		
	Labeled (% N ¹⁵)	K _{II}	Unlabeled (0.37% N ¹⁵)	K _{II}	Ratio of basicities	secondary amine	ammonium chloride	ammonia from the gas phase
1 *	Aniline (2,15)	$5 \cdot 10^{-10}$	α -Naphthyl- amine	$1 \cdot 10^{-10}$	5	2.15	0.67	—
2 ***	Aniline (9,3)	$5 \cdot 10^{-10}$	p-Amino- phenol	$6.6 \cdot 10^{-9}$	13	8.6, 8.6	0.47, 0.49	0.45, 0.45
3	Aniline (9,3)	$5 \cdot 10^{-10}$	p-Amino- phenol	$6.6 \cdot 10^{-9}$	13	9.3, 8.5	0.43, 0.54	0.44, 0.43
4	α -Naphthyl- amine (9,3)	$1 \cdot 10^{-10}$	p-Amino- phenol	$6.6 \cdot 10^{-9}$	66	3.24, 3.25	5.3, 5.4	—
5	Benzamide (9,3)	—	p-Amino- phenol	$6.6 \cdot 10^{-9}$	—	0.44	8.4	—
6	Aniline (3,0)	$5 \cdot 10^{-10}$	n-Butyl- amine	$4 \cdot 10^{-4}$	$8 \cdot 10^5$	2.9, 3.2, 3.0, 2.7, ** 2.9 **	—	—
7	α -Naphthyl- amine (8,4)	$1 \cdot 10^{-10}$	p-Chloro- aniline	$1 \cdot 10^{-10}$	1	0.37, 0.36, 0.39	—	—
8	α -Naphthyl- amine (8,4)	$1 \cdot 10^{-10}$	m-Chloro- aniline	$0.3 \cdot 10^{-10}$	3.3	0.40, 0.40, 0.39	—	—

• • • In the presence of sulfuric acid

(2)

Reaction 4 deserves special attention, where the heavy nitrogen appears in both the p-hydroxydiphenylamine and the ammonium chloride, which indicates that the amino group is cleaved from both of the reaction components. Such a distribution of the N¹⁵ may be caused either by the process going as two independent reactions, or because the intermediate complex decomposes in two directions. We postulate that the main direction of the process, leading to the cleavage in two-thirds of the cases of the heavy amino group from the α -naphthylamine, is associated with the reaction going in accordance with scheme (2). Cleavage in one-third of the cases of the light amino group from the p-aminophenol is evidently associated with the following. It is known [2,3] that the

diaminobenzenes and hydroxyaminobenzenes are hydrolyzed much more easily than is aniline. Thus, hydrolysis of the phenylenediamines and aminophenols at 200°, and lower, results in the formation of the corresponding dihydroxybenzenes in good yields. Consequently, under the conditions used to condense p-aminophenol with amines, i.e., at 210-220°, it is very easy for acid hydrolysis of the p-aminophenol to occur, with the formation of hydroquinone. The latter then condenses with the amine to give the secondary amine. The mechanism of this reaction can be depicted by the following scheme:



The presence of water in the reaction sphere is due to reaction in accordance with scheme (3), and it is always found in the ampoule at the end of experiment. In the condensation of p-aminophenol with α -naphthylamine the addition of water was made for the specific purpose of suppressing the reactivity of the OH group [2].

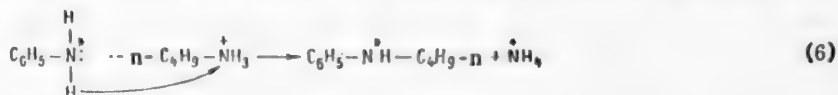
TABLE 2

Heating time	% N ¹⁵	
	N-p-hydroxy-phenyl- α -naphthylamine	ammonium chloride
80 min	2.4	6.4
2 hr	3.1	6.0
10 hr	3.3	5.7

If these reactions actually do take place, then with progress of reaction the ratio of hydroquinone to p-aminophenol and, consequently, the extent to which mechanisms (3)-(5) are involved will increase. This should lead to a change in the amount of heavy nitrogen in the reaction products with time. The results obtained in the kinetic experiments run by us (Table 2) lend support to the theories expressed above. At the start of condensation the process involving cleavage of the light amino group [mechanisms (3)-(5)] plays a lesser role (24%) * than at the end of condensation (34%).

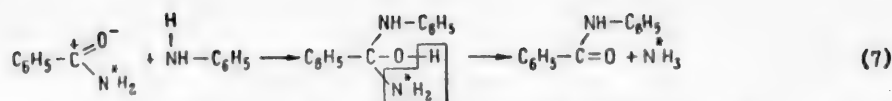
Reactions 2 and 3 (Table 1), where the p-aminophenol loses all of its amino group when condensed with aniline, apparently go in harmony with the hydrolysis mechanism (3)-(5). The fact that p-hydroxydiphenylamine is obtained from hydroquinone and aniline at a higher temperature (290°) [4] casts some doubt on this scheme. To determine if it is possible for these reactions to go under the conditions used in the condensation of the amines, we ran the appropriate experiments. Hydroquinone with aniline and aniline hydrochloride (1:1:1 mole ratio) smoothly gave at 210-220° approximately the same yield of p-hydroxydiphenylamine as was obtained from aniline and p-aminophenol under the same conditions. As a result, the hydrolysis mechanism for the condensation of p-aminophenol with amines seems quite probable to us.

In reaction 6 the amines differ greatly in basicity. The ability to form quinoid forms is weakly expressed in the benzene series, and is not manifested in the given case. The mechanism of the reaction is determined by the large ($8 \cdot 10^5$ times) difference in the dissociation constants. The strong base is present chiefly as the salt, $n\text{-C}_4\text{H}_9\text{NH}_3^+$, which reacts with the free aniline by the nucleophilic substitution mechanism, described earlier [1].



As can be seen from reaction 5 and earlier-published cases [1] (benzamide with aniline or with α -naphthylamine), ammonia is always formed from the nitrogen of the amide when amines are condensed with benzamide. These results are in harmony with the nucleophilic substitution mechanism depicted in scheme (7). Addition of the arylamine group is facilitated by the fact that the carbonyl oxygen, possessing a high electron density, attracts the proton of the amino group; this results in the formation of the ortho-form of the acid amide:

* At the start of condensation, $\frac{2.4 - 0.37}{9.0 - 0.37} \cdot 100 = 24\%$ and, at the end of condensation, $\frac{3.3 - 0.37}{9.0 - 0.37} \cdot 100 = 34\%$ (total effect for the entire reaction time).



Under favorable steric conditions, the cleavage of ammonia occurs with the formation of the acid arylide. This mechanism is analogous to that adopted by Porai-Koshits [5] for the acylation of primary amines. This mechanism also finds analogy in the esterification of alcohols, nitrosation of amines, etc.

The results of our study indicate the absence of nitrogen exchange (or, more correctly, of the NH_2 group) in systems composed of the reacting amines and ammonium chloride under the conditions of the condensation experiments. The results obtained in the system *p*-aminophenol- α -naphthylamine-ammonium chloride do not give any direct indication as to the absence of nitrogen exchange, since distribution of the N^{15} between the reaction products can also be caused by the exchange. However, based on the experiments made in the present study and the analogous condensation experiments made in [1], it is possible to conclude that exchange also fails to occur in this case, and that the appearance of N^{15} in both reaction products is caused by parallel reactions,

EXPERIMENTAL

N^{15} -Benzamide* was obtained by a modification of the method given in [6] from $\text{N}^{15}\text{H}_4\text{NO}_3$ and benzoyl chloride, in 97-99% yield based on the heavy ammonium nitrate taken for reaction. M.p. 126-128°.

N^{15} -Aniline was obtained from N^{15} -benzamide by the Hofmann reaction, in 85-90% of the theoretical yield.

N^{15} - α -Naphthylamine was obtained from N^{15} -ammonium chloride and α -naphthol by heating in an ampoule at 280° with anhydrous sodium acetate and glacial acetic acid [7]. It was purified by steam distillation.

4-Hydroxydiphenylamine. The procedure used to condense aniline with *p*-aminophenol was similar to that developed by Limpricht [8] for obtaining 4-hydroxydiphenylamine from aniline and aminosalicic acid. A mixture of 2 g of *p*-aminophenol sulfate (or the equivalent amount of *p*-aminophenol hydrochloride) and 2.36 g of N^{15} -aniline was heated under reflux in a stream of pure nitrogen for 4 hr at 210-220°. A part of the liberated ammonia was carried out by the nitrogen into a receiver containing dilute hydrochloric acid, while the rest remained in the reaction mass as ammonium chloride.

The unreacted aniline was steam distilled, while the product was extracted from the residue by treating 4-5 times with boiling water.** After standing for several hours, the crystalline *p*-hydroxydiphenylamine was suction-filtered, washed with cold water, and dried in the air. The yield of crude product was 33-36%. Recrystallization from boiling water gave the compound as silver-white leaflets with m.p. 68-69°. The filtrates (first two extractions) from the 4-hydroxydiphenylamine and the acid solution from the receiver were evaporated to dryness. The obtained two samples of ammonium chloride were freed of primary amines by precipitation with sodium cobaltinitrite [9] in alcohol solution (1:1), and then were subjected to isotopic analysis.

4-Benzamidophenol. A mixture of equivalent amounts of *p*-aminophenol hydrochloride (0.24 g) and N^{15} -benzamide (0.2 g) was heated in a sealed ampoule at 180° for 6-7 hr. The reaction mass was extracted with hot water. The ammonium chloride was isolated from the water solution, and then it was freed of amino compounds by precipitation with sodium cobaltinitrite. The crude product was recrystallized from alcohol until a constant melting point of 204° was obtained. The yield of crude product was 0.28 g, or about 80% of the theoretical.

N-4-Hydroxyphenyl- α -naphthylamine. A mixture of 1 g of *p*-aminophenol hydrochloride, 1.1 g of N^{15} - α -naphthylamine, and 1 g of water was heated in a sealed ampoule for 7 hr at 210°. The black, tarry reaction mass was washed with water to extract the ammonium chloride. The hydrochlorides of the primary amines dissolved at the same time. The tarry residue was washed 5 times with hot hydrochloric acid (1:25) to remove the primary amines. The condensation product was extracted 3 times with boiling dilute alcohol (1:5), and after cooling was filtered. The crude N-4-hydroxyphenyl- α -naphthylamine was recrystallized from alcohol (1:4) until

* The details of synthesizing the labeled compounds will be published separately.

** Treatment of the product with dilute hydrochloric acid by the Limpricht technique to remove primary amines was not suitable in our case, since *p*-hydroxydiphenylamine is quite soluble in dilute mineral acids.

a constant melting point of 87-91° was obtained. The yield of pure product was 0.15-0.20 g, or 9-12% of the theoretical.

The water solution of ammonium chloride plus primary amines as impurity was evaporated to dryness, the residue was dissolved in alcohol (1:1), and the ammonium ion was precipitated with sodium cobaltinitrite. The ammonia obtained by decomposition of the precipitate with alkali was absorbed in hydrochloric acid, and then was subjected to isotopic analysis.

n-Butylaniline. The condensation of aniline with n-butylamine gave a complex mixture of various amines: dibutylamine, diphenylamine, butylaniline, dibutylaniline, tributylamine, and unreacted primary amines. In order to increase the amount of butylaniline in the reaction products, it is advisable to run the reaction using a large excess of aniline. After investigating the effect of temperature and the ratio of the components on the yield of butylaniline, we adopted the following optimum procedure.

A mixture of 1.5 g of n-butylamine, 2.58 g of aniline hydrochloride, and 3.72 g of aniline was heated in a sealed ampoule for 17-20 hr at 220-240°. Toward the end of reaction, white crystals of ammonium chloride appeared in the initially homogeneous solution. The oil was filtered from the crystals and then mixed with 130 ml of 10% sodium hydroxide solution. This was followed by the gradual addition of 8 ml of benzenesulfonyl chloride, after which the mixture was gradually heated and mixed until the odor of the benzenesulfonyl chloride disappeared. The mixture of benzenesulfonamides of secondary amines, tertiary amines, and diphenylamine, remaining as an oil, was extracted with ether,* and the ether extract was washed with hydrochloric acid (1:25) to remove the tertiary amines. Then the ether was evaporated, after which the residue was placed in an ampoule with 25% hydrochloric acid and heated for 30 hr at 150°. The mixture after hydrolysis was diluted with water, and the insoluble diphenylamine was extracted with ether. The acid solution was made alkaline and the amines were extracted with ether. The ether solution was then transferred to a separatory funnel containing water, and carbon dioxide was bubbled through the liquid for 40 min. Here the dibutylamine went into the water solution, while the residual n-butylaniline was extracted with ether. The ether solution was then dried over sodium hydroxide, the ether was removed, and the crude n-butylaniline was vacuum distilled. The product was identified from the boiling point and the refractive index. In different experiments we obtained: b.p. from 237° to 242° and n_D^{20} from 1.5374 to 1.5393, instead of 241-242° and 1.5381 (according to the literature).

In several experiments the pure n-butylaniline was also identified using 3-nitrophthalic anhydride [10]. A mixture of stoichiometric amounts of butylaniline and anhydride was heated for 7 min at 145°. The obtained N-butyl-N-phenyl-3-nitrophthalamic acid (III) was recrystallized from alcohol (3:2), and then dried at 100°. M.p. 197°, 201° (according to the literature [10], 204-206°). The hydrolysis of (III) was effected by heating it for 1 hr under reflux with 1:4 hydrochloric acid solution, after which the acid solution was made alkaline, and the free n-butylaniline again extracted.

p- and m-Chlorophenyl- α -naphthylamines [11]. A mixture of 1.3 g of N¹⁵- α -naphthylamine and 0.93 g of either p- or m-chloroaniline (molar ratio 1:1) was heated in a sealed ampoule for 6-7 hr at 170-180°. The ampoule contents, having a dark, tarry appearance, were washed once with boiling water, 3 times with hot dilute hydrochloric acid, again with water, and after drying were vacuum distilled (1-2 mm of Hg). The distilled oil solidified, and was recrystallized 2-3 times from alcohol. The melting points of the compounds purified in this manner were: N-p-chlorophenyl- α -naphthylamine 98° (from the literature [11], 102-103°), and N-m-chlorophenyl- α -naphthylamine 68° (from the literature [11], 72-73°). The yields of the pure products ranged from 0.2 to 0.36 g, or from 10 to 18% of theoretical.

Isotopic analysis of the nitrogen. The samples of ammonium chloride, purified as described above, were decomposed with sodium hypobromite in a Rittenberg apparatus [12], and the obtained nitrogen was collected in a small flask fitted with a stopcock. The organic materials were digested by the Kjeldahl method, using H₂SO₄ and potassium sulfate, and copper oxide as the catalyst. After making alkaline, the ammonia was distilled from the solution into hydrochloric acid, and was obtained as dry ammonium chloride on evaporation of the acid solution. The nitrogen contained in the ammonium chloride was also converted to elemental nitrogen, and the latter was then subjected to isotopic analysis.

* In several experiments this mixture was refluxed for 30 min with sodium ethylate solution to decompose any possibly formed disulfonamides of the primary amines, which are also insoluble in alkali. The results obtained with such a treatment and without it were the same.

The mass-spectrometric analyses were made by measuring the peaks at 28 and 29 (and at 30, when the amount of heavy nitrogen exceeded 5%).

Correction for the amount of air in the sample was made by calculating the value of the oxygen peak at 32. The relative accuracy of the mass-spectrometric measurements was 3-5%.

We wish to thank A. I. Brodskii, Academician of the Academy of Sciences of the Ukrainian SSR, for his assistance in the work reported here.

SUMMARY

The mechanism of the condensation of amines was investigated using the heavy nitrogen isotope. The theory was expressed that the mechanism can be different, depending on the nature of the amines. In the pairs composed of an amine of the benzene series plus naphthylamine the amino group is cleaved from the naphthylamine, probably because of the formation of the quinoid structure in it. In the case of amines differing greatly in basicity, the amino group is cleaved from the stronger base by the nucleophilic substitution mechanism. The condensation of amine with amide proceeds by the nucleophilic substitution mechanism with the formation of the intermediate ortho-form of the acid amide, and for this reason always with cleavage of the amide nitrogen.

It was established that nitrogen exchange is absent under our experimental conditions in systems composed of the reacting amines and ammonium chloride.

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SYNTHETIC DYES

XVII. SYNTHESIS OF AZOMETHINES BY THE CONDENSATION OF

N-ARYLQUINALDINIUM QUATERNARY SALTS WITH α -NITROSO- β -NAPHTHOL

G. T. Pilyugin and S. V. Shinkorenko

Chernovitskii State University

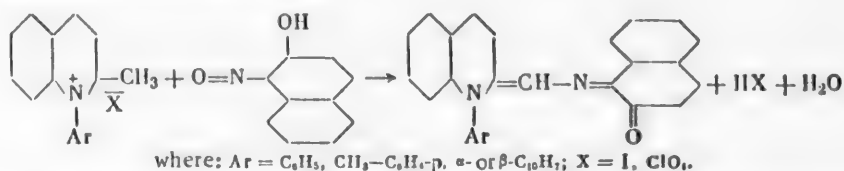
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May, 1960

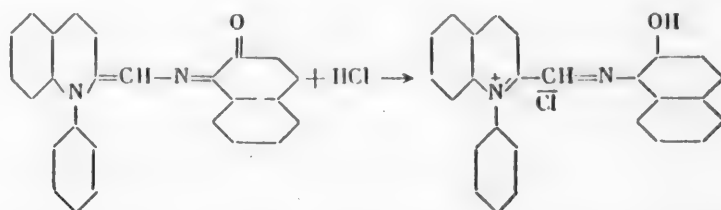
Original article submitted April 15, 1959

Quaternary salts of N-arylquinolinium bases containing an active methyl group in the α -position to the nitrogen heteroatom are characterized by the methyl group entering readily into many reactions with orthoesters, aromatic aldehydes, ketones, diazo compounds, nitroso compounds, etc. [1-4].

Continuing our study of azomethine compounds, we reacted some of the new salts obtained by us with nitrosonaphthol, and here we obtained azomethine intraionoid dyes, which were characterized. The formation of these dyes went in accordance with the following scheme:



The structure of the obtained compounds was verified by the analytical and spectrophotometric data. It was observed that the more deeply colored dyes — the free bases — when acidified in alcohol solution show a sharp heightening in the color, which corresponds to a transition of the free base to the salt.



Intraionoid dyes possess the ability to change color, depending on the solvent [5]. The azomethine dyes synthesized by us also possess the property of solvatochromism, which can be seen from the absorption curves and the data given in the table, where the absorption maxima in various solvents are shown.

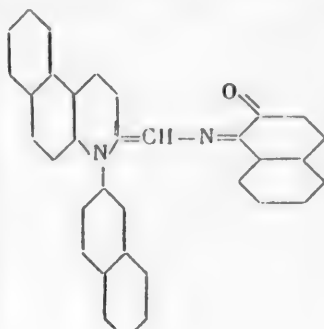
From the data given in the table it can be seen that all of the compounds, taken separately in either ethyl or methyl alcohol, possess relatively close absorption maxima, whereas in the other solvents, except carbon tetrachloride, the dyes with a quinoline perichrome each have two absorption maxima, of which those in the long-wave region are shifted toward the red portion of the spectrum by a substantial amount (20-40 m μ). The presence of substituents in the quinoline ring and on the nitrogen heteroatom has little effect on the color. In methyl alcohol, when compared to ethyl alcohol, a hypsochromic shift of the absorption maximum by 13-17 m μ is observed. The appearance of two absorption maxima and a bathchromic shift both indicate that the formation of compounds with different energy levels occurs when the dye and solvent molecules are excited, and that excitation of the vibrational levels in the conjugated double bonds occurs simultaneously with the electron transitions [6]. The absorption curves for all of the listed compounds, when dissolved in either methyl or ethyl alcohol or in carbon tetrachloride, show only one absorption maximum (Fig. 1).

Absorption Maxima of Dyes in Various Solvents

Expt. No.	Formula of dye	Absorption maxima of the dyes (in mμ)						
		ethanol	methanol	chloroform	benzene	acetone	di-oxane	carbon tetrachloride
1 *		660	647	644, 685	642, 688	633, 669	636, 679	645
2		657	640	646, 683	649, 690	634, 667	641, 682	649
3		665	652	644, 685	641, 684	633, 671	637, 680	643
4 *		659	644	695	659, 704	678	654, 692	664
5		658	642	694	660, 706	676	656, 692	666

* These dyes were described earlier [4].

(continued)

Expt. No.	Formula of dye	Absorption maxima of the dyes (in mμ)						
		ethanol	methyl alcohol	chloroform	benzene	acetone	dioxane	carbon tetrachloride
6		661	646	695	660, 708	675	656, 694	663

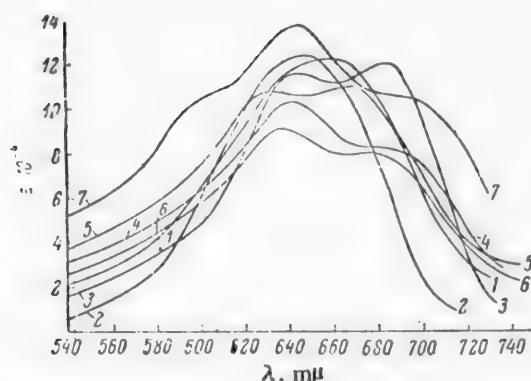


Fig. 1. Absorption spectra of 2-oxonaphthyl-1-(1-phenyl-2-quinoline)azomethine: 1) in ethyl alcohol; 2) in methyl alcohol; 3) in chloroform; 4) in benzene; 5) in acetone; 6) in dioxane; 7) in carbon tetrachloride.

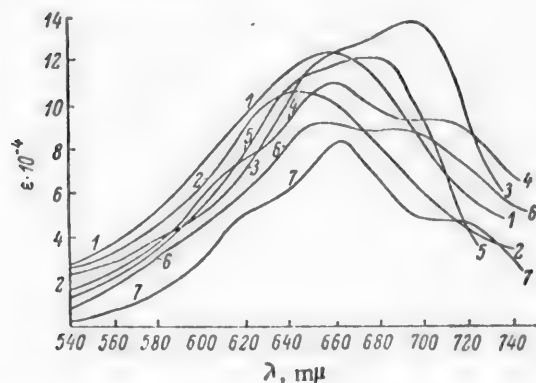


Fig. 2. Absorption spectra of 2-oxonaphthyl-1-(1-phenyl-5,6-benzo-2-quinoline)azomethine: 1) in ethyl alcohol; 2) in methyl alcohol; 3) in chloroform; 4) in benzene; 5) in acetone; 6) in dioxane; 7) in carbon tetrachloride.

The dyes in which one of the perichromes is the benzoquinoline nucleus, taken in all of the solvents except the alcohols, show a bathochromic shift of the absorption maxima when compared with the azomethines containing a quinoline perichrome. In chloroform and acetone the compounds with a quinoline perichrome give absorption curves with two maxima, while the dyes with a benzoquinoline structure have only one absorption maxima (Fig. 2).

It should be mentioned that the synthesized azomethine dyes are extremely light sensitive. Thus, it was observed that their colored solutions in the indicated solvents became completely colorless in 10-15 hr. This process is especially rapid in carbon tetrachloride solution, where decolorization occurs within 30 min.

EXPERIMENTAL

2-Oxonaphthyl-1-[1-(1-p-tolyl)-6-methyl-2-quinoline]azomethine. A mixture of 0.5 g of 1-(p-tolyl)-6-methylquinazolinum perchlorate and 0.25 g of α -nitroso- β -naphthol was dissolved in 20 ml of hot alcohol. Then 2-3 drops of piperidine were added to the hot solution, and this caused the solution to change instantly from a light-yellow to a blue-green color. The reaction mass was heated to the boil, and then 2-3 ml of water was added. On cooling, the azomethine crystallized as lustrous golden scales. Yield 0.45 g (77%). After recrystallization from alcohol, m.p. 177-178° (decomp.). The absorption curve was taken with an automatic-recording SF-2M spectrophotometer. The absorption maximum in alcohol lies at 656 mμ.

Found %: N 7.42, 7.00. $C_{23}H_{22}ON_2$. Calculated %: N 6.96.

2-Oxonaphthyl-1-[1-(p-tolyl)-5,6-benzo-2-quinoline]azomethine. A mixture of 0.5 g of

1-(p-tolyl)-5,6-benzoquinaldinium iodide and 0.21 g of α -nitroso- β -naphthol was dissolved in 10 ml of hot alcohol, followed by the addition of 2 drops of piperidine to the hot solution, and here the color changed from a brown to a blue-green. Then 5 ml of alcohol and 2 ml of water were added to the reaction mass. The reaction mass on standing deposited a dark-blue powder, while some of the product also separated as tiny glistening crystals. Yield 0.35 g (66%). Recrystallization from alcohol gave the compound as a dark-green, finely crystalline powder with m.p. 210-211°. The absorption maximum in ethanol lies at 658 m μ .

Found %: N 6.83, 6.42. $C_{31}H_{22}ON_2$. Calculated %: N 6.38.

2-Oxonaphthyl-1-[1-(α -naphthyl)-2-quinoline]azomethine. A mixture of 0.5 g of 1-(α -naphthyl)quinaldinium perchlorate and 0.22 g of α -nitroso- β -naphthol was dissolved in 15 ml of hot alcohol, and then 1-2 drops of piperidine were added. The reaction mass soon assumed a blue-green color. On adding 2-3 ml of water and rubbing with a rod, the reaction product crystallized as a lustrous bronze powder. Yield 0.34 g (64%). Recrystallization from alcohol gave the compound as bronze needles with m.p. 190-191°. The absorption maximum in ethanol lies at 666 m μ .

Found %: N 6.43, 6.61. $C_{30}H_{20}ON_2$. Calculated %: N 6.59.

2-Oxonaphthyl-1-[1-(β -naphthyl)-5,6-benzo-2-quinoline]azomethine. One gram of 1-(β -naphthyl)-5,6-benzoquinaldinium iodide and 0.55 g of α -nitroso- β -naphthol were each dissolved in 10 ml of alcohol. The alcohol solutions were then poured together, 2-3 drops of piperidine were added, which caused the color of the reaction mass to become blue-green, and then the reaction product began to separate as a tar, which, after adding 10 ml of alcohol and stirring, changed to a finely crystalline powder. Yield 0.74 g (62.7%). Recrystallization from alcohol gave the compound as bronze needles with m.p. 189-190°. The absorption maximum in ethanol lies at 661 m μ .

Found %: N 6.30, 5.83. $C_{34}H_{22}ON_2$. Calculated %: N 5.90.

SUMMARY

1. It was shown that the reaction of N-arylquinaldinium quaternary salts with nitrosonaphthol yields azomethine dyes.
2. The azomethine dyes change their color when dissolved in different solvents; this is confirmed by their absorption spectra, taken in the visible region.

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DIRECTED SYNTHESIS OF ISOMERIC QUATERNARY SALTS IN THE PHENAZINE SERIES

Yu. S. Rozum

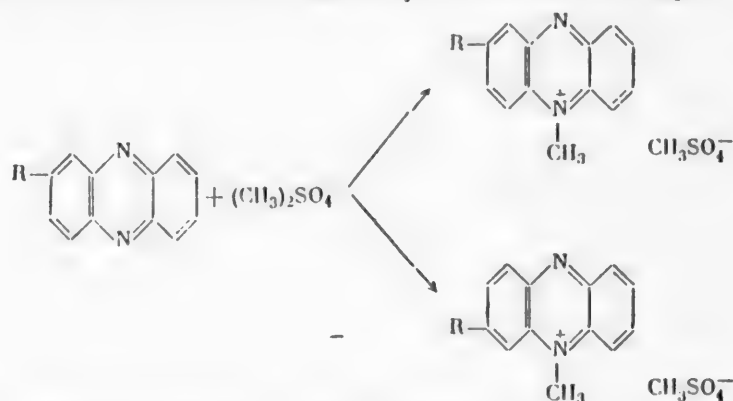
Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR

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The quaternary salts of phenazine and its various derivatives are used in the synthesis of certain antibiotics, azine dyes, and analytical reagents. Because of the uniform distribution of the electron densities between the two nitrogen atoms, the unsubstituted phenazine gives only one quaternary salt. For the monosubstituted phenazines, and especially for those which contain substituents exerting electronic effects on the process of salt formation, it is possible for the formation of two isomeric quaternary salts to occur, for example:



In this reaction, the positive alkyl ion is an acceptor of electrons, and attack by the alkylating agent is directed mainly toward the nitrogen atom of the unsymmetrically substituted phenazine molecule with the higher electron density. Actually, a mixture of the two isomeric salts is always formed here. The preparative separation and identification of these salts are associated with great difficulties, at times insurmountable.

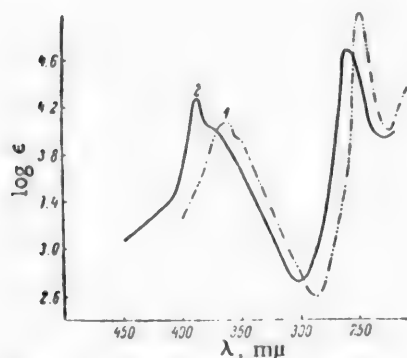


Fig. 1. Absorption spectra: 1) phenazine; 2) 9-methylphenazinium perchlorate (in alcohol).

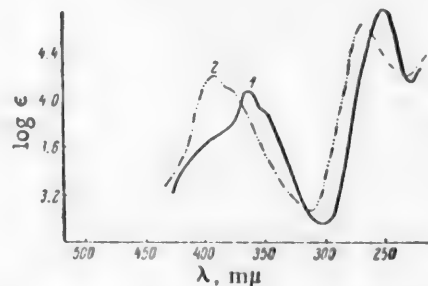


Fig. 2. Absorption spectra: 1) 1-phenylphenazine; 2) 1-phenyl-9-methylphenazinium perchlorate (in alcohol).

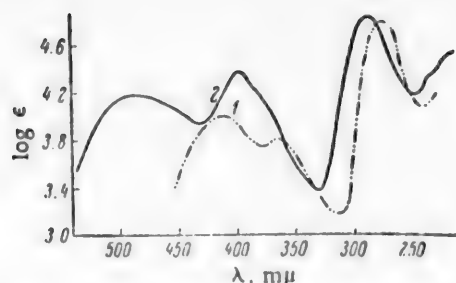


Fig. 3. Absorption spectra: 1) 2-phenyl-6-methoxyphenazine; 2) 2-phenyl-6-methoxy-10-methylphenazinium perchlorate (in alcohol).

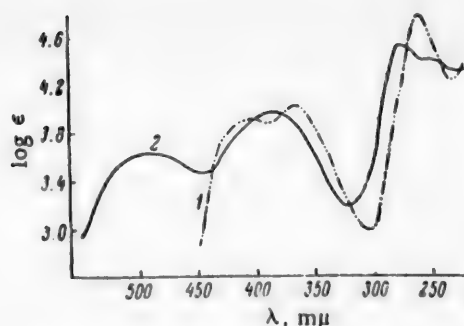


Fig. 4. Absorption spectra: 1) 1-phenyl-7-methoxyphenazine; 2) 1-phenyl-7-methoxy-10-methylphenazinium perchlorate (in alcohol).

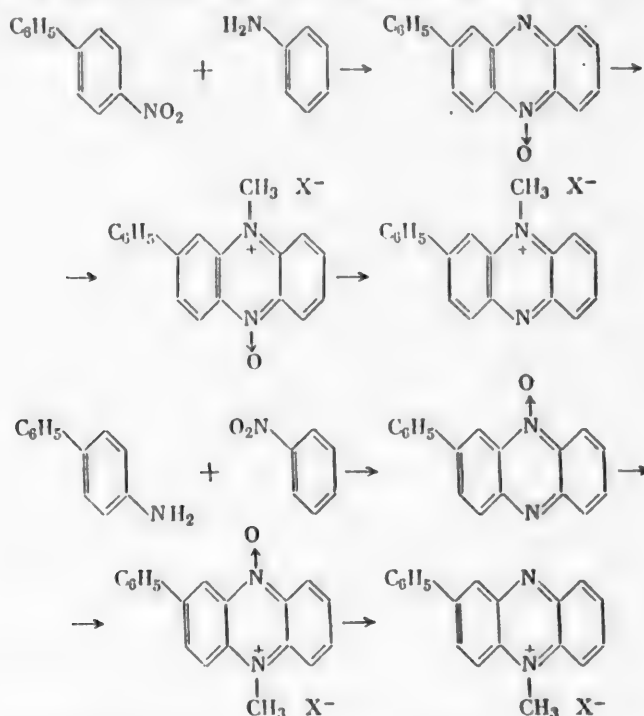
TABLE 1

Quaternary Phenazinium Salts (Perchlorates), Obtained by the Reduction of Quaternary Salts of Phenazine N-Oxides with Zinc Dust

Substituents in the phenazinium salt molecule	Decomp. temp.	Yield (%)	Absorption maxima (mμ)	Found %		Formula	Calc. %	
				N	Cl		N	Cl
9-Methyl	201°	57	259, 384	9.76, 9.69	12.08, 11.90	$C_{13}H_{11}O_4N_2Cl$	9.51	12.05
2-Chloro-9-methyl	176	85	263, 397	8.40, 8.25	21.56, 21.39	$C_{13}H_{10}O_4N_2Cl_2$	8.51	21.58
2-Chloro-10-methyl	222	25	264, 392	8.54	21.52, 21.71	$C_{13}H_{10}O_4N_2Cl_2$	8.51	21.58
2-Methoxy-9-methyl	205	49	265, 391, 442	8.58, 8.66	11.49, 11.40	$C_{14}H_{13}O_5N_2Cl$	8.63	10.94
2-Methoxy-10-methyl	188	78	266, 395, 446	8.93, 8.62	10.96, 11.04	$C_{14}H_{13}O_5N_2Cl$	8.63	10.94
2-Chloro-6-methoxy-9-methyl	211	32	271, 388, 455	7.96, 7.81	19.65, 19.82	$C_{14}H_{12}O_5N_2Cl_2$	7.80	19.54
1-Phenyl-9-methyl	196	16	268, 394	7.34, 7.19	9.57, 9.69	$C_{19}H_{15}O_4N_2Cl$	7.55	9.58
1-Phenyl-10-methyl	217	49	250, 267, 387	7.57, 7.73	—	$C_{19}H_{15}O_4N_2Cl$	7.55	—
2-Phenyl-9-methyl	237	30	276, 417	7.52, 7.58	9.53, 9.71	$C_{19}H_{15}O_4N_2Cl$	7.55	9.58
2-Phenyl-10-methyl	205	87	276, 409	7.50, 7.59	9.54, 9.33	$C_{19}H_{15}O_4N_2Cl$	7.55	9.58
2-Phenyl-6-methoxy-9-methyl	165—167	8	279, 410, 491	7.42, 7.44	8.73, 8.72	$C_{20}H_{17}O_5N_2Cl$	7.00	8.86
1-Phenyl-7-methoxy-10-methyl	238	37	276, 385, 490	6.98, —	9.06, 9.08	$C_{20}H_{17}O_5N_2Cl$	6.99	8.86

A method for obtaining phenazine quaternary salts of precisely determined structure is described in this paper. The ability discovered by us of phenazine and quinoxaline N-monooxides reacting with dimethyl sulfate to form the quaternary salts of the N-oxides [1] served as the lead for developing this method. Utilizing the established rule [2], on the basis of which, in the alkaline condensation of aromatic nitro and amino compounds (by the Wohl method) it is possible to predetermine the location of the oxide oxygen in the phenazine N-oxide by proper choice of the reacting components, we prepared a series of isomeric N-oxides of phenazine derivatives. These oxides were obtained so that one of the two centers of basicity in the phenazine molecule (either the 9- or the 10-nitrogen atom) was linked to the oxygen, while the other remained exposed to the action of the alkyl ion. Then the obtained quaternary salts of the phenazine N-oxides were reduced with zinc dust to the true quaternary

salts of the bases. The method for the directed synthesis of the quaternary salts of the phenazine quaternary salts can be illustrated by the scheme for the preparation of the two isomeric salts of 2-phenylphenazine.



As a result, a path is uncovered for the separate preparation of quaternary salts of normal structure (salts where the alkyl ion is attached to the nitrogen atom with a high electron density), as well as of salts of anomalous structure (salts where the alkyl ion is attached to the nitrogen atom with a low electron density). The quaternary salts of anomalous structure are somewhat less stable than the salts of normal structure; The decomposition temperatures of the first are lower than those of the second. The described method was tested on various phenazine derivatives (Table 1). All of the quaternary salts prepared by this method were characterized by their melting points and decomposition temperatures, and by their ultraviolet absorption spectra in alcohol solutions, in concentrations ranging from 10^{-4} to 10^{-5} M. In salt formation the spectrum of the free base is shifted toward longer wavelengths, and the bands in the long-wave region are intensified; in this connection, the short-wave bands become weaker. The same changes also take place when the other phenazine derivatives are converted to the salts (Figs. 1 and 2).

The absorption spectra of the quaternary salts of phenazine and its various derivatives show two groups of bands: The very strong bands lie in the short-wave region of the spectrum in the vicinity of 250 m μ , while the weak bands are found in the long-wave region around 400 m μ . In the case of some of the derivatives (most frequently for the disubstituted derivatives), a third band appears in the vicinity of 500 m μ , as illustrated, for example, by 2-phenyl-6-methoxy-10-methylphenazinium perchlorate and 1-phenyl-7-methoxy-10-methylphenazinium perchlorate (Figs. 3 and 4).

The N-monooxides of the substituted phenazines (Table 2) were obtained by the standard method of alkaline condensation of the appropriate nitro and amino derivatives of benzene or diphenyl. Examples of obtaining the isomeric 9- and 10-oxides of 2-phenyl-6-chlorophenazine are given in the experimental section. All of the phenazine N-oxides were purified chromatographically on aluminum oxide from benzene solution. The phenazine N-monooxides are easily distinguished from the corresponding bases by the following criteria.

a) With the exception of the compounds where steric hindrance is present, the phenazine monooxides exhibit, in contrast to the bases corresponding to them, a strong fluorescence in either benzene or chloroform solution when irradiated with a quartz lamp equipped with an ultraviolet light filter. Some of the phenazine oxides also fluoresce in the daylight. An especially strong fluorescence is observed for those phenazine N-oxides

TABLE 2

Alkaline Condensation of Aromatic Nitro Compounds with Aromatic Amines. Phenazine N-Oxide Derivatives



Starting compounds		Name of phenazine N-oxide	Yield (%)	Melting point of decomp. (d) temp.	Absorption maxima (mμ)	Found N (%)	Formula ^a	Calc. N (%)
A	B							
Aniline	Nitrobenzene	Phenazine 9-oxide	14	224°	265, 361, 380, 395, 418	13.97, 13.85	C ₁₂ H ₈ ON ₂	14.28
o-Toluidine	Nitrobenzene	1-Methylphenazine 10-oxide	11	195	251, 266, 381, 396, 418	13.74, 13.78	C ₁₃ H ₁₀ ON ₂	13.33
p-Anisidine	Nitrobenzene	2-Methoxyphenazine 9-oxide	12	179	271, 360, 378, 413, 436	12.53, 12.42	C ₁₃ H ₁₀ O ₂ N ₂	12.39
p-Chloroaniline	Nitrobenzene	2-Chlorophenazine 9-oxide	16.4	178-179	271, 365, 380 (t) **, 386, 399, 422	11.85, 11.71	C ₁₂ H ₇ ON ₂ Cl	12.14
Aniline	p-Nitrochlorobenzene	2-Chlorophenazine 10-oxide	12	176-178	268, 387, 406, 428	12.47, 12.51	C ₁₂ H ₇ ON ₂ Cl ^a	12.14
p-Anisidine	p-Nitrochlorobenzene	2-Methoxy-6-chlorophenazine 9-oxide	23	204	277, 360, 380, 418, 442	10.77, 10.79	C ₁₃ H ₉ O ₂ N ₂ Cl ^b	10.74
Aniline	o-Nitrophenyl	1-Phenylphenazine 9-oxide	1.3	172	272, 365, 382, 408, 427	10.05, 10.09	C ₁₈ H ₁₂ ON ₂	10.29
o-Aminodiphenyl	Nitrobenzene	1-Phenylphenazine 10-oxide	10	200-202	270, 295, 364, 382, 410, 430	10.35, 10.15	C ₁₈ H ₁₂ ON ₂	10.29
p-Anisidine	o-Nitrophenyl	1-Phenyl-7-methoxyphenazine 9-oxide	11.4	199	247, 276, 364, 382, 410, 445	9.23, 9.14	C ₁₉ H ₁₄ O ₂ N ₂	9.27
o-Anisidine	o-Nitrophenyl	1-Phenyl-5-methoxyphenazine 9-oxide	7.5	206-207	265, 350, 364, 418	9.29, 9.18	C ₁₉ H ₁₄ O ₂ N ₂	9.27
p-Aminodiphenyl	Nitrobenzene	2-Phenylphenazine 9-oxide	16	135 199-201 (d)	288, 397, 434	10.38, 10.18	C ₁₈ H ₁₂ ON ₂	10.24
Aniline	p-Nitrophenyl	2-Phenylphenazine 10-oxide	0.7	168 200-203 (d)	268, 287, 398	10.25, 10.29	C ₁₉ H ₁₂ ON ₂	10.29
p-Anisidine	p-Nitrophenyl	2-Phenyl-6-methoxyphenazine 10-oxide	10.5	188 200-211 (d)	246, 294, 370, 388, 424, 447	9.36, 9.40	C ₁₉ H ₁₄ O ₂ N ₂	9.27
p-Aminodiphenyl	p-Nitrochlorobenzene	2-Phenyl-6-chlorophenazine 9-oxide	6.6	204.5 220 (d)	242, 291, 380, 395, 418, 442	8.84, 8.88	C ₁₈ H ₁₁ ON ₂ Cl ^c	
p-Chloroaniline	p-Nitrophenyl	2-Phenyl-6-chlorophenazine 10-oxide	4.0	189 218-220 (d)	245, 276, 292, 385, 399, 432	9.09, 9.17	C ₁₈ H ₁₁ ON ₂ Cl ^d	
p-Aminodiphenyl	p-Nitrophenyl	2,6-Diphenylphenazine 9-oxide	0.7	218-221 (d)	266, 308, 385, 404, 425, 448	8.02, 8.17	C ₂₁ H ₁₆ ON ₂	8.04

^a Found %: Cl a) 15.39, 15.55; b) 13.84, 13.78; c) 11.65, 11.69; d) 11.81, 11.66. Calculated %: Cl a) 15.40; b) 13.47; c) 11.53; d) 11.58.

** 1- inflections on the absorption curve.

TABLE 3

Quaternary Salts (Perchlorates) of Phenazine and Quinoxaline N-Oxides

Phenazinium (ph) and quinoxalinium (q) perchlorates	Melting or decomp. point	Yield (%)	Appearance and color of crystals	Absorption maxima (mμ)	Found %		Formula	Calc. %	
					N	Cl		N	Cl
10-Methyl (ph) 9-oxide	214*	81	Orange prisms	250 (l) • 279, 349, 388, 450, 473 265, 278, 385	8.56, 8.97	11.72, 11.67	C ₁₃ H ₁₁ O ₃ N ₂ Cl	9.01	11.43
1,9-Dimethyl (ph) 10-oxide	200	53	Pale orange needles		—	10.71, 10.64	C ₁₄ H ₁₃ O ₃ N ₂ Cl	—	10.94
2,10-Dimethyl (ph) 9-oxide	196	41	Orange needles	255 (l) 263, 281, 303	8.59, 8.49	10.77, 10.89	C ₁₄ H ₁₃ O ₃ N ₂ Cl	8.63	10.94
2-Methoxy-10-methyl (ph) 9-oxide	204	41	Orange needles	266, 290 (l) 394, 446	8.55, 8.67	10.28, 10.65	C ₁₄ H ₁₃ O ₃ N ₂ Cl	8.22	10.42
2-Methoxy-9-methyl (ph) 10-oxide	198	40	Red needles	225, 266, 290, 392, 404, 470	8.13, 7.89	10.39, 10.60	C ₁₄ H ₁₃ O ₃ N ₂ Cl	8.22	10.52
2-Chloro-10-methyl (ph) 9-oxide	220	60	Orange needles	252, 264, 284, 380 (l) 395	8.01, 7.88	20.80, 20.73	C ₁₃ H ₁₀ O ₃ N ₂ Cl ₂	8.11	20.52
2-Chloro-9-methyl (ph) 10-oxide	223	70	Orange plates	252, 265, 277 (l) 284, 380 (l) 398	8.14, 7.83	20.52, 20.73	C ₁₃ H ₁₀ O ₃ N ₂ Cl ₂	8.11	20.52
2-Chloro-6-methoxy-9-methyl (ph) 10-oxide	213	76	Red hexagonal plates	274, 397, 455	7.54, 7.50	18.88, 18.71	C ₁₄ H ₁₂ O ₆ N ₂ Cl ₂	7.47	18.93
1-Phenyl-10-methyl (ph) 9-oxide	197	43	Red-brown needles	260, 387	7.31, 7.41	9.17, 9.14	C ₁₉ H ₁₅ O ₃ N ₂ Cl	7.24	9.18
1-Phenyl-9-methyl (ph) 10-oxide	217	72	Red plates	251, 285, 398, 502	7.38, 7.49	9.26, 9.40	C ₁₉ H ₁₅ O ₃ N ₂ Cl	7.24	9.18
1-Phenyl-7-methoxy-10-methyl (ph) 9-oxide	228	50	Red-brown prisms	262, 383, 490	6.85, 6.99	8.69, 8.73	C ₂₀ H ₁₇ O ₆ N ₂ Cl	6.72	8.52
1-Phenyl-5-methoxy-10-methyl (ph) 9-oxide	190	44	Lustrous orange plates	287, 390	6.68	8.73, 8.78	C ₂₀ H ₁₇ O ₆ N ₂ Cl	6.72	8.52
2-Phenyl-10-methyl (ph) 9-oxide	224	85	Bright red needles	240, 292, 417	7.22, 7.20	9.29, 9.27	C ₁₉ H ₁₅ O ₃ N ₂ Cl	7.24	9.19
2-Phenyl-9-methyl (ph) 10-oxide	216	48	Red needles	282, 430	7.30, 7.24	—	C ₁₉ H ₁₅ O ₃ N ₂ Cl	7.24	—
2-Phenyl-6-methoxy-9-methyl- (ph) 10-oxide	242	50	Red needles	260, 412 (l), 423, 295	6.72, 6.72	8.58, 8.70	C ₂₀ H ₁₇ O ₆ N ₂ Cl	6.72	8.52
2-Phenyl-6-chloro-10-methyl (ph) 9-oxide	236	70	Dark red plates	245, 298, 416, 466	6.92, 7.11	17.06, 16.82	C ₁₉ H ₁₄ O ₃ N ₂ Cl ₂	6.65	16.86
2-Phenyl-6-chloro-9-methyl (ph) 10-oxide	210	93	Orange needles	288, 418, 480	6.87, 6.96	17.05, 17.12	C ₁₉ H ₁₄ O ₃ N ₂ Cl ₂	6.65	16.86
1-Phenyl-6-methoxy-3-methyl (ph) 10-oxide	206	71	Orange plates	263, 375, 420	6.72, 6.77	8.53, 8.54	C ₂₀ H ₁₇ O ₆ N ₂ Cl	6.72	8.52
2,3-Diphenyl-4-methyl (q) 1-oxide	175-177	95	Yellow needles	250, 270 (l), 350	6.55, 6.45	8.37, 8.57	C ₂₁ H ₁₇ O ₃ N ₂ Cl	6.78	8.60
2,3-Diphenyl-4,6- (or 4,7-) dimethyl (q) 1-oxide	220	85	Yellow prisms	208, 250, 263, 358	6.59, 6.43	—	C ₂₂ H ₁₉ O ₃ N ₂ Cl	6.56	—
2,3-Acenaphthylene-4-methyl (q) 1-oxide	246	75	Yellow needles	236, 335, 346, 384	7.12, 6.98	9.30, 9.40	C ₁₉ H ₁₃ O ₃ N ₂ Cl	7.07	9.23
2,3-Acenaphthylene-4,6- (or 4,7-) dimethyl (q) 1-oxide	232	43	Yellow tablets	240, 315, 327, 340-400 (l)	6.93, 7.02	9.01, 9.21	C ₂₀ H ₁₅ O ₃ N ₂ Cl	7.03	8.91

*1- inflections on the absorption curve.

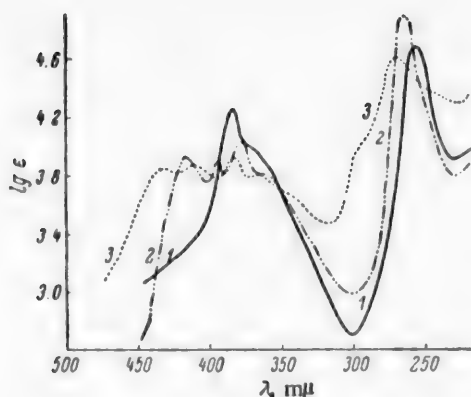


Fig. 5. Absorption spectra: 1) phenazine; 2) phenazine 9-oxide; 3) 1-phenylphenazine 10-oxide (in alcohol).

containing an OCH_3 group in the 2-position. The greatest luminescence is observed in the case of 1-phenyl-7-methoxyphenazine 10-oxide. The isomeric 9-oxide is completely non-fluorescent.

b) Besides the melting points, the phenazine N-monooxides are also characterized by their decomposition temperatures, which at times coincide with the melting points of a given compound, or lie above them.

c) The absorption spectra of the phenazine N-monooxides are characterized by having a group of bands (from 3 to 5) in the 350-450 $\text{m}\mu$ region which, on reduction, merge into one slight band, lying near 360 $\text{m}\mu$. This portion of the spectrum is shown in Fig. 5 for phenazine, its N-oxide, and for 1-phenylphenazine 10-oxide.

The preparation of the quaternary salts of the phenazine N-oxides, as well as their reduction, has been reported in part in previous papers [1,3]. The data on the quaternary salts of the phenazine N-oxides are given in Table 3.

EXPERIMENTAL

Formation of N-monooxides of phenazine derivatives. The standard procedure [3] was used to obtain the N-monooxides by the alkaline condensation of nitro and amino derivatives of benzene or diphenyl in the presence of powdered KOH in boiling benzene. The synthesis of the 9- and 10-oxides of 2-phenyl-6-chlorophenazine is described below.

2-Phenyl-6-chlorophenazine 9-oxide. A mixture of 51 g of p-aminodiphenyl, 63 g of p-nitrochlorobenzene, and 120 g of powdered KOH was refluxed with mechanical stirring in 500 ml of benzene for 22 hr. The benzene layer was decanted, and the residue in the reactor was extracted with boiling benzene (3×250 ml). The benzene extracts were combined, washed with water, and steam-distilled. The residue, containing 2-phenyl-6-chlorophenazine, its N-oxide, 4-phenyl-4'-chloroazobenzene, and other condensation products was dried, dissolved in benzene (500 ml), and chromatographed on aluminum oxide (column 900×40). From the third zone (counting from the bottom), showing strong fluorescence under a quartz lamp equipped with an ultraviolet light filter, we isolated 6.1 g of 2-phenyl-6-chlorophenazine 9-oxide (yellow needles). The N-oxide is readily soluble in aromatic solvents, chloroform, dioxane, and alcohol, is difficultly soluble in petroleum ether, and is practically insoluble in water. The compound exhibits a bright-yellow fluorescence in chloroform solution.

2-Phenyl-6-chlorophenazine 10-oxide was obtained in the same manner as the preceding from 80 g of p-nitrodiphenyl, 38 g of p-chloroaniline, and 120 g of KOH in 500 ml of benzene (20 hr). We isolated 4.92 g of 2-phenyl-6-chlorophenazine 10-oxide (yellow needles) from the third zone of the chromatogram. The compound exhibits yellow fluorescence in CHCl_3 solution.

Formation of quaternary salts of phenazine N-oxides. The following technique was used to convert the N-oxides of phenazine and its various derivatives to the quaternary salts of the N-oxides. The weighed sample of phenazine oxide (about 0.3-0.5 g) was dissolved in 1 ml of pure, dry nitrobenzene at $110-115^\circ$ in a test tube fitted with a thermometer; then the dialkyl sulfate was added to the obtained solution, and the temperature was raised to $125-130^\circ$ (oil bath). Usually, the mixture assumed a bright-red color at this temperature. The start of salt formation was detected by the sharp rise in temperature due to the exothermic reaction. To avoid overheating the salt, the test tube was removed from the bath at this point. The end of reaction is easily established by moistening a test drop of the mixture with water on a watch glass: The methyl sulfates of the phenazine N-oxides are completely soluble in water. When the reaction is carried out successfully, the salt formation, when using the alkyl and alkoxy derivatives of the N-oxides, is complete in 3-8 min; in the case of the chloro derivatives, where the basicity of the salt-forming nitrogen is greatly lowered, the reaction is ended in 10-12 min; approximately the same length of time is required for the phenyl derivatives of the phenazine N-oxides. The reaction mass is colored dark red; if the salt is overheated, the product assumes a brownish color. At the same time, the

yield of the salt is lowered, and the reaction product requires extensive purification. At times the quaternary salt deposits as a thick slurry of fine crystals during the time of reaction. In such cases, the reaction mass is cooled, and the quaternary salt is transferred to a small filter, where it is washed with dry toluene and ether. Usually the quaternary salt is obtained in a very pure state as uniform needles, plates, or prisms. If the reaction mass fails to crystallize when cooled, it is stirred thoroughly with toluene to extract the nitrobenzene and excess dialkyl sulfate. This extraction of the impurities with fresh toluene is continued until the quaternary salt deposits as a thick sticky mass on the walls of the test tube. The extraction is ended by washing with ether. The obtained quaternary salt can then be recrystallized from a little alcohol with the addition of activated carbon, or it can be dissolved in 5-7 ml of water, and after treatment with activated carbon it can be precipitated by the addition of sodium perchlorate.

All of the quaternary salts of the substituted phenazine N-oxides are colored either a bright orange or red, and in this way are easily distinguished from the salts of the corresponding bases, which are colored either yellow or dark yellow. The quaternary salts of the phenazine N-oxides can be stored for a long time (8-12 months) without change; they are all soluble (the methyl sulfates are very soluble, the iodides are more difficultly soluble, and the perchlorates are difficultly soluble) in water, alcohol, and dioxane; they are capable of being reduced to the true quaternary salts of the corresponding bases. The preparation of the new quaternary salts of the N-oxides of 2-phenyl-6-chlorophenazine is described below.

2-Phenyl-6-chloro-10-methylphenazinium 9-oxide perchlorate. To a solution of 0.31 g of 2-phenyl-6-chlorophenazine 9-oxide in 1 ml of nitrobenzene at 115-116°, in an oil bath, was added 1 ml of neutral dimethyl sulfate, after which the temperature was raised to 130-135°, and the reaction mixture was kept at this temperature for 25 min. The reaction mass had a dark cherry-red color. A crystalline precipitate failed to deposit. The quaternary salt was washed, as indicated above, with toluene, and then with ether. Yield 0.30 g. The salt was recrystallized from 2 ml of alcohol, using activated carbon (obtained as dark-red plates).

2-Phenyl-6-chloro-9-methylphenazinium 10-oxide perchlorate. The compound was obtained in the same manner as the above, from 0.31 g of 2-phenyl-6-chlorophenazine 10-oxide and 1 ml of dimethyl sulfate, omitting the nitrobenzene, at 130-132° for 15 min. Yield 0.40 g. The compound was converted in the usual manner to the perchlorate, which was obtained as orange needles (from a mixture of alcohol and dioxane).

General directions for the reduction of the quaternary salts of the N-oxides of phenazine and its derivatives. A 7-10% water solution of the phenazinium N-oxide methosulfate is prepared for the reduction; then the zinc dust, taken in an amount approximately equal to 50% of the weight of quaternary salt taken for reduction, is added at one time, and the rise in temperature is followed by constantly stirring the mixture with a rod thermometer. Due to the exothermic nature of the reaction, the temperature rises by 15-20° in 3-5 min. The end of the reduction is determined by the color of the solution changing from an orange to a yellow or dark yellow. The solution is then filtered rapidly from the zinc dust; this operation should not be protracted, since the obtained quaternary salt of the base is reduced further to the insoluble dihydro product, causing a decrease in the yield of the quaternary salt of the base. Several drops of 10% sodium perchlorate are added to the filtrate. The precipitate of N-methylphenazinium perchlorate is filtered, washed with water, and then with a little cold alcohol and ether.

Well-purified quaternary salts of the N-oxides of the phenazine derivatives should be taken for the reduction, so that only one recrystallization of the reduced salt is necessary later; this circumstance is quite important in obtaining the so-called anomalous quaternary salts, characterized by a low stability. The technical details of the reduction are described in previous papers [1,3].

The author is indebted to A. I. Kiprianov for his interest in the work.

SUMMARY

A route for the synthesis of phenazinium quaternary salts of a given structure was developed. The compounds synthesized in this paper include some new N-monooxides of phenazine derivatives, their quaternary salts, and also the quaternary salts of a number of phenazine and quinoxaline bases. A study was also made of the properties and ultraviolet absorption spectra of these compounds.

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CONCERNING p,p'-DIPHENYLSTILBENE

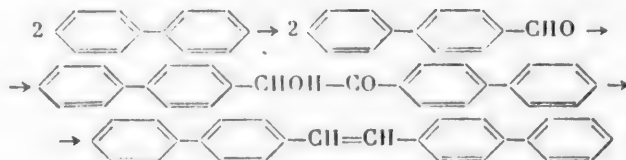
E. E. Baroni and K. A. Kovyrzina

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At the present time, scintillation counters have found widespread acceptance for the measuring of nuclear radiations. To increase the scintillation efficiency of the scintillator, it has proved expedient to introduce two organic luminescent compounds into the plastic, one of which plays the role of the main activator, while the second is added in small amounts and plays the role of a coactivator in shifting the fluorescence spectrum and, at the same time, it functions to increase substantially the total efficiency of the scintillator.

A whole series of statements exist in the literature on the successful use of p,p'-diphenylstilbene as a coactivator [1-5]. However, the synthesis of this compound is not described in the general literature. We worked out a synthesis for this compound, using biphenyl as the starting material. The carbonylation [6,7] of biphenyl yields p-biphenylcarboxaldehyde, which then, by benzoin condensation (similar to the condensation of benzaldehyde [8]), is converted to p,p'-diphenylbenzoin. The diphenylbenzoin is not reduced by methods similar to the known methods for obtaining stilbene from benzoin [9-11], evidently because of the large steric hindrance. We worked out a new way of reducing the diphenylbenzoin in a hydrogen atmosphere with zinc dust in the presence of concentrated hydrochloric acid. Here it was established that, depending on the conditions of the reduction process, it is possible to obtain both of the geometric isomers of p,p'-diphenylstilbene. When ordinary zinc dust is used, the end reaction product proves to be the cis-diphenylstilbene, obtained as a white crystalline compound. However, when amalgamated zinc dust is used, the end reaction product is the trans-diphenylstilbene, which is obtained as greenish-yellow lustrous scales.



The existence of two geometric isomers of the diphenylstilbene is supported by the different catalytic hydrogenation rate. Paal and Schiedewitz [12] established that usually the cis-form hydrogenates more rapidly than the trans-compound. The hydrogenation curves of both compounds are shown in Fig. 1.

Isomers corresponding to the cis- and trans-forms of compounds should be quite different in their fluorescent properties [13-17], since a different spatial configuration of the atomic groups in the stereoisomers exerts an effect on the interaction of the π -electrons [18] and, consequently, on the position of the spectral absorption bands, and also on the value of the absorption coefficient. A planar arrangement of the atoms in the molecule gives the greatest shift of the spectral bands toward longer wavelengths and the strongest absorption. When bulky

* Original Russian pagination. See C.B. translation.

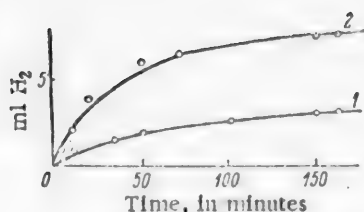


Fig. 1. Hydrogenation rate of the cis- and trans-isomers of p,p'-diphenylstilbene: 1) trans-; 2) cis-.

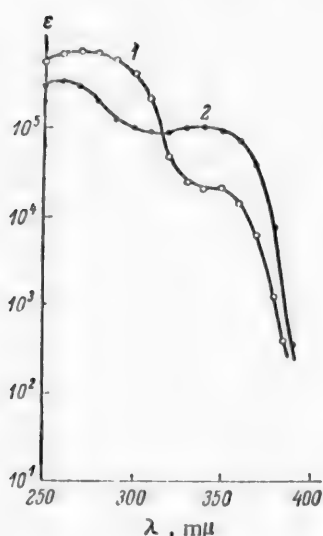


Fig. 2. Absorption spectra of the cis- and trans-isomers of p,p'-diphenylstilbene in dioxane (10^{-3} g/ml): 1) cis-; 2) trans-.

groups are present in the molecule, the cis-configuration unavoidably leads to a disruption of the coplanarity of the molecule. Because of this, the absorption band of the cis-form will lie in the region of shorter wavelengths, and the absorption maximum will lie lower than for the trans-form, as is observed for stilbene and other compounds [13, 14, 19, 20]. The absorption spectra of the cis- and the trans-diphenylstilbene are shown in Fig. 2.

A visual study of the fluorescence of the isomeric forms of p,p'-diphenylstilbene in the crystalline state yielded some interesting results. It proved that the trans-form exhibits an intense blue luminescence, while the cis-form shows a violet luminescence that, in intensity, is much weaker than that displayed by the trans-compound. Both isomers give a violet luminescence in organic solvents, but here again that of the trans-form is more intense.

Both isomers show an entirely different character when contained in plastic scintillators. The scintillator containing the trans-diphenylstilbene is more efficient than the one containing the cis-isomer. The results of measuring the efficiency of plastic scintillators containing the two diphenylstilbenes will be published separately.

The trans-configuration can be converted to the cis-form by heating in nitrobenzene, and the same effect is observed on long exposure of the solid samples to ultraviolet light.

EXPERIMENTAL

p,p'-Diphenylbenzoïn. A mixture of 7 g of p-phenylbenzaldehyde [6,7], 70 ml of 96% alcohol, and 1 g of sodium cyanide in 10 ml of water was heated in a round-bottomed flask under reflux for 30 min. In approximately 5-10 min a yellow precipitate began to deposit from the hot solution, and rapidly increased in bulk. After cooling, the precipitate was filtered, washed on the filter with 100 ml of 50% aqueous alcohol, and dried. Yield 6.31 g (90%). Recrystallization from alcohol gave the compound as fine, colorless crystals with m.p. 161-162°.

Found M 370.1. $C_{26}H_{20}O_2$. Calculated M 364.4.

Trans-p,p'-diphenylstilbene. Into a three-necked round-bottomed flask, fitted with a mechanical stirrer, a gas-outlet tube descending nearly to the bottom of the flask, a dropping funnel, and a reflux condenser, was charged 1.13 g of pure diphenylbenzoïn, 6.59 g of amalgamated zinc dust, and 20 ml of alcohol. Then a stream of hydrogen was passed through the mixture, (heated to the boil), and at the same time 13.1 ml of concentrated hydrochloric acid was added slowly in drops. Here the reaction mass, a thick white slurry, turned yellow, and after 10-15 min changed to a greenish-yellow precipitate. The reaction time was 1 hr. Then the reaction mass was cooled and diluted with water, after which the precipitate was carefully suction-filtered (most of the unreacted zinc dust remained on the bottom of the flask), washed on the filter with water, and dried. Then the precipitate was recrystallized from benzene and the zinc dust was removed. The solution on cooling deposited a greenish-yellow substance as glistening scales. Three recrystallizations from benzene gave the pure compound with m.p. 204-204.5°. Yield 0.82 g (82%).

Found %: C 93.39; H 6.75. M 326.2. $C_{26}H_{20}$. Calculated %: C 93.92; H 6.08. M 332.4.

The catalytic hydrogenation was run by the Paal and Schiedewitz procedure [12,21,22]. As catalyst we used palladium deposited on barium sulfate; this was prepared by the Paal procedure [23,24]. The hydrogenation conditions were: 0.2 g of $BaSO_4$ catalyst \equiv 0.002 g of Pd; 0.2083 g of compound in 10 ml of alcohol (15°, 770 mm); time of hydrogenation 6 hr, 45 min. The course of the hydrogenation is shown in Fig. 1.

Cis-p,p'-diphenylstilbene. With vigorous stirring and heating to the boil, a stream of hydrogen chloride and hydrogen was passed through a mixture composed of 1.5 g of p,p'-diphenylbenzoin, 1 g of zinc dust, and 19 ml of alcohol. The gas mixture was obtained by the action of concentrated hydrochloric acid on zinc turnings, with heating. Here the white, doughy mass gradually changed to a yellow precipitate, which could be separated easily from the alcohol solution. The reaction time was 2.5-3 hr. The reaction mass, after cooling, was diluted with water, and the precipitate was filtered, washed with water, and dried. Recrystallization from benzene, followed by sublimation in a high vacuum (10^{-4} mm) at 200° , gave the compound as white crystals with m.p. 221 to 222° . The yield of pure product was 1.1 g (84.6%).

Found %: C 93.96; H 6.11. M 336.29. $C_{26}H_{20}$. Calculated %: C 93.92; H 6.08. M 332.43.

The catalytic hydrogenation was run in the same manner as for the trans-diphenylstilbene: 0.2 g of $BaSO_4$ catalyst \equiv 0.002 g of Pd; 0.2013 g of compound in 10 ml of alcohol (14° , 773 mm); time of hydrogenation 2 hr, 45 min. The course of the hydrogenation is shown in Fig. 1.

p,p'-Diphenylstilbene is difficultly soluble in all organic solvents. The mixture of trans- and cis-diphenylstilbene melts at $207-211^{\circ}$.

SUMMARY

A method was worked out for obtaining p,p'-diphenylstilbene in good yield. The cis- and trans-isomers were isolated in the pure state.

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SPATIAL STRUCTURE AND REACTIVITY

XVI. KINETICS OF REACTION OF AMINO DERIVATIVES OF DIPHENYLMETHANE AND DIBENZYL WITH p-NITROBENZOYL CHLORIDE AND PICRYL CHLORIDE

L. M. Litvinenko and N. F. Levchenko

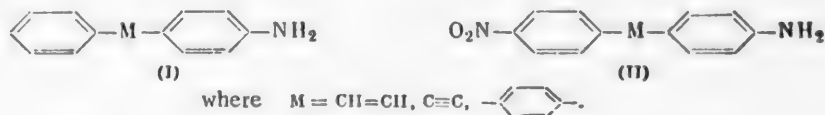
Khar'kov State University

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In recent years, employing the technique of kinetic measurements, we investigated the ability of substituents to transfer their influence in molecular systems composed of two benzene rings linked by unsaturated hydrocarbon bridges (I and II) [1-3].



The ratio of the rate constants for the reaction of amino and aminonitro derivatives with p-nitrobenzoyl chloride or with picryl chloride can serve as a quantitative measure of such an influence, i.e., $K_I/K_{II} = f$.

In this paper we report the data obtained in studying the kinetics of reacting p-nitrobenzoyl chloride and picryl chloride with the analogous derivatives of diphenylmethane ($M = \text{CH}_2$) and dibenzyl ($M = \text{CH}_2 - \text{CH}_2$) in benzene solution under conditions completely identical with previous ones. This makes it possible to elucidate the character of the influence exerted by substituents of different benzene rings on each other in the case where these rings are connected by unsaturated hydrocarbon bridges.

Regarding the transfer of the effects of substituents in systems of the indicated type, we were unable to find any literature information that was based on chemical methods of study. However, in studying the absorption spectra of aromatic derivatives of methane, V. F. Lavrushin and N. A. Valyashko [4,5] came to the conclusion that the methane carbon atom is not an insulator here, but instead serves as a link joining the benzene rings into one reacting system. A compilation of the literature supporting this point of view is also given in [5]. V. A. Izmail'skii, G. V. Alekseeva, and R. S. Tsekanskii [6,7], who studied the color of a number of diphenylmethane derivatives, came to a similar conclusion. But Gillam and Stern [8] present facts illustrating that, in contrast to such binuclear hydrocarbons as biphenyl and stilbene (where, judging by the optical properties, the presence of a strong conjugation effect between the benzene rings is clearly manifested), in diphenylmethane and dibenzyl the methylene bridges are practically complete insulators of the indicated effect. Brode [9] also regards the methylene groups as functioning as insulators of the conjugation between two chromophores.

EXPERIMENTAL

1. Preparation and Purification of Starting Materials

The benzene, p-nitrobenzoyl chloride [11], and picryl chloride [1] were purified as indicated earlier.

4-Aminodiphenylmethane (I, $M = \text{CH}_2$). To 16 g of 4-nitrodiphenylmethane [12] dissolved in 180 ml of hot methyl alcohol was added 22.5 ml of hydrazine hydrate, and then the Raney nickel was added gradually, observing here the operational procedure that was described in detail earlier [13] (regarding the use of methyl alcohol for this purpose, see [10, 14, 15]). When the nitrogen evolution had ceased, indicating the end of reaction, the still warm solution was filtered to remove catalyst and the solvent was distilled off as completely as possible. The oily residue was treated with concentrated hydrochloric acid. The obtained solid product was filtered and washed with ether (by the technique of efficient trituration and subsequent suction-filtration). The yield of the hydrochloride was almost quantitative. The salt was recrystallized twice from dilute hydrochloric

acid (1:1) using activated carbon, and then the same number of times from 10% sulfuric acid. Trituration of the salt under a layer of warm aqueous ammonia solution gave the free base as an oily product, which crystallized after it was washed with water and cooled. The amine was recrystallized once each from dilute methyl alcohol (2:1 by volume) and from petroleum ether. After long drying in a vacuum oven at 30°, m.p. 36-36.5°.

4-Amino-4'-nitrodiphenylmethane (II, $M = CH_2$) was synthesized by our earlier-described method [16]. The crude amine sulfate was recrystallized 3 times from 10% sulfuric acid (using activated carbon). The free base was isolated by treatment with aqueous ammonia, after which it was recrystallized twice from aqueous methyl alcohol (the compound was dissolved in boiling alcohol and then hot water was added in drops until a permanent turbidity appeared), and then once each from anhydrous methyl alcohol and from benzene. After drying for 3 hr in a vacuum oven at 65°, m.p. 98°.

4-Aminodibenzyl (I, $M = CH_2 - CH_2$) was obtained by the method given in [16]. The crude hydrochloride was recrystallized twice from dilute hydrochloric acid (1:2) using activated carbon, and then twice each as the free base from aqueous methyl alcohol (using the same procedure as in the case of recrystallizing the 4-amino-4'-nitrodiphenylmethane) and from petroleum ether.* After drying in a vacuum oven at 35-40°, m.p. 51-52°.

4-Amino-4'-nitrodibenzyl (II, $M = CH_2 - CH_2$) was also synthesized by the method given in [16]. The crude amine sulfate was recrystallized 3 times from 10% sulfuric acid, after which the salt was converted through the free base to the hydrochloride, which was also recrystallized 3 times from dilute (1:2) hydrochloric acid (using activated carbon the first time). The free base was obtained in the usual manner, and then it was recrystallized twice from methyl alcohol and once from benzene. The compound, after drying at 65° in a vacuum oven for 3 hr, had m.p. 138.5-139°.

2. Procedure and Results of Kinetic Measurements

The procedure for measuring the reaction rate, and also the methods used to calculate the second-order reaction rate constants, the energy of activation (E), the frequency factor (A), and the entropy of activation (ΔS^\ddagger) were described earlier [1]. In all of the experiments, the initial concentration of the p-nitrobenzoyl chloride (a) was always half the initial concentration of the amine (b).

The numerical data obtained for the reactions of the amino derivatives of diphenylmethane and dibenzyl are presented in Table 1, where k_i is the average value of the rate constant for a given time interval t_i with number of measurements n_i . The average values of the reaction yield for n_i measurements are given in the second column in this table. The principal data on the kinetics of the reactions investigated in the present paper are summarized in Table 2, as are also some of the values obtained by us for earlier-studied reactions. K is the average value of the rate constant for all Σn_i measurements.

Some of the experiments, run with various initial concentrations of the starting components, revealed that the rate constants of the investigated reactions, as had also been established earlier for other similar cases [3,10], hardly change with the dilution. Thus, for example, for the reaction of 4-aminodiphenylmethane with picryl chloride at $a = 0.00125$ and $b = 0.0025$, $K_{25^\circ} = 0.338$ liter/mole/sec, while at $a = 0.0025$ and $b = 0.005$, $K_{25^\circ} = 0.341$ liter/mole/sec.

DISCUSSION OF RESULTS**

A comparison of the results obtained in studying the reactions of aniline and of the 4-amino derivatives of various binuclear hydrocarbons reveals that substituents introduced in the para-position of aniline fall into the following series when arranged in the order of decreasing electron-donor (and increasing electron-acceptor) properties: $C_6H_5 - CH_2 - CH_2 - > C_6H_5 - CH_2 - > H > C_6H_5 - \equiv C_6H_5 - C_6H_4 - > C_6H_5 - CH = CH - > C_6H_5 - C \equiv C -$. The first two members in this series are donors, while the others are acceptors of electrons. If a p-NO₂ group is present in the benzene rings of the hydrocarbon substituents, then the indicated series suffers only one change: in its electron-acceptor properties the para-substituent on the biphenyl derivative (p-NO₂ - C₆H₄ - group) becomes one of the strongest and, in this respect, yields only to the analogous tolan derivative (p-NO₂ - C₆H₄ - C \equiv C - group). The latter is explained by the fact that of all of the examined binuclear molecular systems that of biphenyl, as will be shown, possesses the greatest ability to conduct the effect of 4,4'-substituents.

*Using this solvent makes it possible to remove efficiently any impurities insoluble in saturated hydrocarbons, by the technique of hot filtration.

** See summary in Table 2.

TABLE 1

Kinetics of Reaction of Amino Derivatives of Diphenylmethane and Dibenzyl with p-Nitrobenzoyl Chloride (PNEC) and Picryl Chloride (PC)

Expt. No.	25°			50°		
	t_1 (in min)	Yield (in %)	k_1 (in liter per mole/sec)	t_1 (in min)	Yield (in %)	k_1 (in liter per mole/sec)
4-Aminodiphenylmethane + PNEC						
1	5	26.5	0.969	2	23.7	2.15
2	8	37.6	1.01	3	31.5	2.12
3	12	47.7	1.02	5	43.5	2.13
4	17	55.3	0.977	8	55.9	2.19
5	26	65.3	0.974	15	70.4	2.19
4-Amino-4'-nitrodiphenylmethane + PNEC						
6	15	20.7	0.233	8	22.1	0.489
7	30	33.3	0.233	12	31.0	0.517
8	50	46.0	0.229	20	41.3	0.487
9	75	56.7	0.234	34	54.8	0.492
10	115	65.4	0.220	50	65.3	0.521
4-Aminodiphenylmethane + PC						
11	5	19.5	0.325	2	19.2	0.823
12	8	28.5	0.334	4	33.2	0.860
13	13	40.2	0.347	6	41.7	0.825
14	19	49.0	0.339	9	52.8	0.860
15	35	64.2	0.334	16	66.5	0.857
4-Amino-4'-nitrodiphenylmethane + PC						
16	30	20.0	0.0559	13	22.5	0.154
17	50	30.3	0.0582	20	30.4	0.151
18	80	40.3	0.0565	30	40.5	0.157
19	120	50.0	0.0559	45	52.0	0.163
20	180	60.5	0.0571	70	62.0	0.161
4-Aminodibenzyl + PC						
21	4	19.8	0.413	2	25.6	1.19
22	9	36.0	0.419	3	33.3	1.15
23	13	45.3	0.427	5	46.3	1.19
24	20	55.1	0.412	7	54.5	1.18
25	30	65.2	0.419	11	64.9	1.16
4-Amino-4'-nitrodibenzyl + PC						
26	14	20.6	0.124	5	20.0	0.346
27	23	29.8	0.124	10	33.8	0.352
28	36	40.1	0.125	15	44.1	0.363
29	53	49.7	0.125	23	54.9	0.365
30	100	65.6	0.128	35	65.0	0.366

Remarks: 1. In experiment Nos. 1-10, $a = 0.000625$ and $b = 0.00125$; in the remaining experiments $a = 0.00125$ and $b = 0.0025$ mole/liter. 2. In experiment Nos. 4, 14, 15, and 24, at 50°, $n_1 = 3$; in all of the other experiments $n_1 = 2$.

TABLE 2


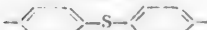




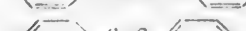


Summarized Data on the Kinetics of Reaction of Amines with p-Nitrobenzoyl Chloride and Picryl Chloride

Amine	Electro- philic agent*	K_{25}° (in liter/mole/sec)	K_{50}° (in liter/mole/sec)	E (in cal/mole)	log A	$\Delta S^{\#}$ (cal/deg/mole)
	PNBC PC	0.990 \pm 0.020 0.338 \pm 0.007	2.16 \pm 0.03 0.847 \pm 0.015	5600 7000	4.37 4.08	-40.6 -39.2
	PNBC PC	0.228 \pm 0.005 0.0567 \pm 0.0007	0.501 \pm 0.012 0.138 \pm 0.004	6000 7850	3.78 4.51	-43.3 -40.0
	PC	0.418 \pm 0.006	1.17 \pm 0.01	7900	5.40	-35.9
	PC	0.126 \pm 0.002	0.358 \pm 0.007	8000	4.96	-37.9
	PNBC PC	0.280 \pm 0.012 0.0619 \pm 0.0020	0.755 \pm 0.012 0.222 \pm 0.007	7600 9800	5.01 5.16	-37.7 -33.3
	PNBC PC	0.0573 \pm 0.0032 0.0121 \pm 0.0005	0.126 \pm 0.005 0.0128 \pm 0.0009	6100 9700	3.18 5.18	-46.0 -36.9
	PNBC PC	0.0406 \pm 0.0006 0.00823 \pm 0.00016	0.126 \pm 0.003 0.0315 \pm 0.0011	8300 10300	4.69 5.45	-39.1 -35.6
	PNBC PC	0.0100 \pm 0.0005 0.00177 \pm 0.00010	0.0304 \pm 0.0013 0.00701 \pm 0.00029	8500 10600	4.24 4.98	-41.2 -37.8
	PC	0.0685 \pm 0.003	0.204 \pm 0.006	8400	4.96	-37.9
	PC	0.0300 \pm 0.0013	0.107 \pm 0.004	9700	5.61	-34.9
	PNBC PC	0.533 \pm 0.010 0.0744 \pm 0.0021	1.11 \pm 0.02 0.235 \pm 0.003	5600 8800	3.85 5.32	-42.8 -36.2
	PNBC PC	0.0505 \pm 0.0011 0.00548 \pm 0.00018	0.118 \pm 0.003 0.0205 \pm 0.0009	6500 10000	3.46 5.15	-44.7 -37.1
	PNBC PC	0.580 \pm 0.018 0.120 \pm 0.002	0.394 \pm 0.005	9100	5.75	-34.3

*PNBC = p-nitrobenzoyl chloride; PC = picryl chloride.

TABLE 3

Values of f Factors for Various Molecular Systems

Molecular systems	f_{25}^* for reaction	
	with p-nitrobenzoyl chloride	with picryl chloride
	6250	17100
	23.8	—
	12.1	—
	10.6	13.6
	4.34	5.96
	4.89	5.12
	4.06	4.65
	—	3.32
	—	2.28

transmission of the effect of the 4'-substituent from one benzene ring to the other. The fact mentioned above—that the $C_6H_5-CH_2-CH_2$ group exerts a stronger electron-donor effect than the $C_6H_5-CH_2$ group—can be explained in the same way.

It is interesting that when the benzene rings in the molecular system of biphenyl are separated by either an oxygen or a sulfur bridge, we even observe an increase in the value of f , which, as was already indicated [10, 18, 19], is associated with a transfer of the reactivity of substituents in such systems in accordance with the mechanism of p, π -conjugation [17, 20]. In a paper reviewing some of the work done in our laboratory, the opinion was expressed by E. N. Gur'yanova [21] that the effect of enhancing the influence exerted by the 4'-nitro group on the 4-amino group, when going from the molecular system of biphenyl to the diphenyl oxide and diphenyl sulfide systems, is determined primarily not by any special properties of the bridge heteroatoms (being expressed in their ready inclusion in the general system of conjugation with the benzene rings), but rather it is determined by the fact that the last two molecular systems, in contrast to the linear biphenyl system, have an angular structure. Reserving the right soon to give a full answer to the remarks of E. N. Gur'yanova, we cannot help but mention here that the sharp quantitative distinction in the character of the interaction of the NO_2 and NH_2 groups in molecular systems containing bridging heteroatoms, and in the diphenylmethane system, which also has an angular structure, is explained, as can now be seen from the data obtained by us, by only one reason and, specifically, by the chemical nature of the bridging unit, which in this way removes the basis of the objections of our opponent. Incidentally, the linear molecular system of tolan also fails to show any advantages as regards the transmission of the electronic effects of substituents over the stilbene system which, being of the same type as the tolan system, still is not linear [3].

A comparison of the kinetic data for molecular systems in which the benzene rings are joined by bridge groupings composed of two links reveals that in going from the saturated ethane grouping in the dibenzyl system to the unsaturated groupings in the stilbene and tolan systems, the ability to transmit the effect of substituents increases very slightly, although in the last two systems the classical case of π, π -conjugation [17, 20] of multiple bonds is represented, while in the dibenzyl system it is broken by the saturated bridge grouping. In their ability to transmit, the molecular systems of stilbene and tolan do not differ quantitatively from the diphenylmethane system, despite the fact that in diphenylmethane the π, π -conjugation between the benzene rings is also broken by the bridge grouping. In this case, we have an example where rupture of a continuous conjugated system of bonds is compensated by a shortening of the distance between the interacting substituents.

Thus, the gradual separation of the NO_2 and NH_2 groups of a constantly longer system of conjugated bonds (transition from benzene to biphenyl, stilbene, tolan, and p-terphenyl) leads to a sharp damping of the effect

The values of f have been assembled in Table 3, from which it can be seen that in the molecular system of diphenylmethane the effect exerted by the nitro group on the reactivity of the amino group is expressed less sharply than in the case of the biphenyl system. This is undoubtedly associated with the fact that the CH_2 grouping functions as an insulator, weakening the interaction of the benzene rings. However, the fact that the rate with which 4-aminophenylmethane reacts with both electrophilic reagents changes substantially when the 4'-nitro group is introduced serves as evidence that quite substantial inductive effects are transmitted through the methylene grouping, and these, in the given case, are apparently coupled to a certain degree with the mechanism for the σ, π -conjugation of the σ -electrons of the CH bonds of the indicated grouping with the π -electrons of the benzene rings [17]. Two methylene groupings in the molecular system of dibenzyl assure a further weakening of the

exerted by the first group on the reactivity of the second. If the separating bridge with multiple bonds, included in the total conjugated system, is replaced by a shorter bridge, but one that breaks the continuous system of conjugation (the CH_2 grouping when compared with all of the unsaturated groupings, or the $\text{CH}_2 - \text{CH}_2$ grouping when compared with the phenylene grouping), then, despite the latter circumstance, the factor of shortening the distance is the deciding one in determining the character of the interaction of the indicated 4,4'-substituents. Besides this, if it is considered that a change in the number of bonds in the bridge grouping (transition from the dibenzyl system to stilbene and tolan) also does not cause a sharp enhancement of the effect of the 4'-nitro group on the reactivity of the 4-amino group, then, on the basis of all that has been said above, it must be concluded that the well-known rule of vinylogy (according to which, in conjugated systems, the influence of substituents is transmitted to the reaction center without noticeable diminution [22,23]) fails to find support, at least for the case of molecular systems similar to those discussed here, when a quantitative study is made of the problem.

Regarding the energy parameters of the reactions investigated in this paper, it can be stated that the reactions go at low values of effective E and ΔS^\ddagger , in which connection somewhat higher values of the indicated constants prevail when the reactions are run with picryl chloride than when run with p-nitrobenzoyl chloride. It should also be mentioned that for the reactions where different amines are reacted with the same electrophilic reagent, the transition from one amino derivative to another is, in general, accompanied by a noticeably smaller change in ΔS^\ddagger than in E . It is also necessary to bear in mind that for those reactions discussed in the present paper, where the amino derivatives contain very long and complex molecules, it is possible for a hindered internal rotation around the single bonds connecting different parts of the molecules (see [11]), and present to variable degree in the indicated compounds, to exert important influence on the dependence of the rate constant on the temperature, which complicates treating the results from the standpoint of changes in E and ΔS^\ddagger under the influence of structural factors.

SUMMARY

1. The kinetics of reacting 4-aminodiphenylmethane, 4-amino-4'-nitrodiphenylmethane, and the analogous derivatives of dibenzyl with p-nitrobenzoyl chloride and picryl chloride was examined.

2. It was confirmed that the methylene grouping in the molecular system of diphenylmethane functions as an insulator in the transmission of the effects of the substituents from one benzene ring to the other. This property appears to an even greater degree in the case of separating the benzene rings by two methylene groupings in the molecular system of dibenzyl.

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SYNTHESES IN THE PHENOTHIAZINE SERIES

III. AMINES OF THE PHENOTHIAZINE SERIES. PART I

V. A. Skorodumov, É. N. Il'chenko, and S. V. Zhuravlev

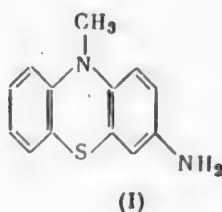
Institute of Pharmacology and Chemotherapy, Academy of Medical Sciences of the USSR

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Phenothiazine derivatives include a large number of physiologically active compounds that have found clinical use as agents acting on the central nervous system and as antihistaminics. All of these compounds, except for a dialkylaminoalkyl (at times, a heteroalkyl) group in the 10-position of the phenothiazine ring, either do not have any other substituents, or else they have a chlorine, acetyl, or some other group in the 2-position.** In order to study the relationship between pharmacological activity and molecular structure, we synthesized a number of phenothiazine derivatives in which the dialkylaminoalkylamino group is located on one of the carbon atoms in the ring.



The present paper deals with the synthesis of one of the starting materials and, specifically, of 10-methyl-3-aminophenothiazine (I). The reasons for selecting this compound were the following. Of the four possible isomers of the aminophenothiazine, not one has been accurately characterized up to now. Apparently the reason for this lies in the difficulty of synthesizing some of them, and also because the 1- and 3-isomers are exceedingly prone to oxidation, as a result of which the corresponding ortho- and para-quinoid compounds are formed. The repeatedly synthesized 3-aminophenothiazine [2-7] was studied only as the leuco base of the dye obtained by its

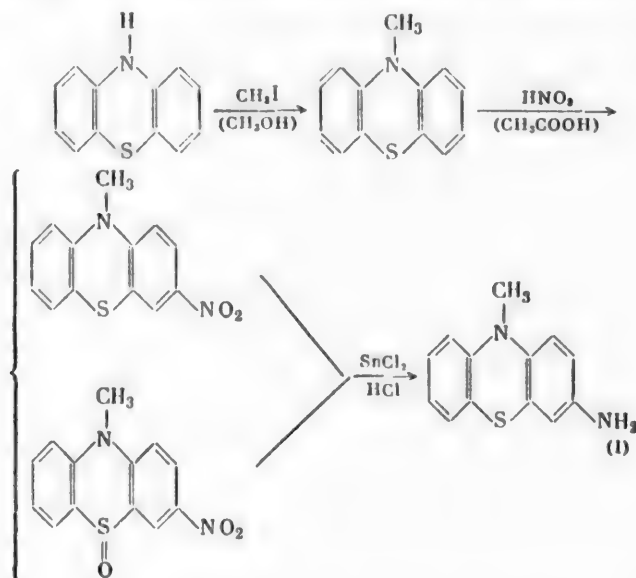
*Original Russian pagination. See C.B. translation.

**For the numbering in the phenothiazine system see [1].

oxidation. (I) was synthesized by Kehrmann [8], but it was characterized only as the acetyl derivative. The introduction of an alkyl substituent in the 10-position makes the compound quite resistant to oxidation, and prevents the formation of the quinoid grouping, which is confirmed by the synthesis of 10-ethyl-3-aminophenothiazine [9]. We became convinced that it is impossible to avoid the formation of colored quinoid products in the synthesis of 3-aminophenothiazine when we repeated the work of Bernthsen [2] and of Kehrmann [10].

Three main methods exist for the synthesis of phenothiazines substituted in the ring on the amino group: 1) thionation of the appropriate aminodiphenylamine in which the amino group is substituted, with subsequent cleavage of the protecting group; 2) reduction of the appropriate nitro derivatives of the phenothiazines or of the nitro-5-oxophenothiazines (here it should be mentioned that when the reduction of 3-nitro-5,5-dioxophenothiazine is attempted only the nitro group is reduced with the formation of 3-amino-5,5-dioxophenothiazine [11]); and, 3) employing the Smiles rearrangement [12]. The last method involves using difficultly available starting materials. Our attempts to use the first of the indicated methods lacked success right from the start, since it proved impossible to obtain the starting 4-nitrodiphenylamine in satisfactory yield by the Goldberg method [13], either by heating p-nitroaniline with bromobenzene in the presence of potassium carbonate, copper, and iodine, or by heating p-nitrochlorobenzene with aniline in the presence of sodium acetate or copper, iodine, and potassium carbonate (even Hantzsch [14] reported on the lack of success using the Goldberg method).

Our goal was achieved using the following procedure. Phenothiazine was methylated with methyl iodide to 10-methylphenothiazine. The nitration of 10-methylphenothiazine with nitric acid in acetic acid solution gave a mixture of 10-methyl-3-nitrophenothiazine and 10-methyl-3-nitro-5-oxophenothiazine. The reduction of this mixture with tin and hydrochloric acid gave us 10-methyl-3-aminophenothiazine, which was characterized by preparing various derivatives. The indicated processes are outlined in the scheme.



Based on the reasons given by Bernthsen [2,15] for the structure of 3-nitrophenothiazine, and also the statements made by Kehrmann [8] regarding the identity of the N-methyl derivative obtained by the reaction of methyl iodide with 3-nitro-5-oxophenothiazine and the nitration product of 10-methylphenothiazine, we assign structure (I) to the compound synthesized by us. Proof of the validity of the proposed structure (I) will be the subject of a separate paper.

EXPERIMENTAL

10-Methylphenothiazine. A mixture of 150 g of phenothiazine, 114 g of methyl iodide, and 150 ml of methanol was heated in a 400-ml steel bomb on the boiling water bath for 10 hr. The bomb contents quickly crystallized after dumping. Recrystallization from alcohol gave 136-142 g (85-89% yield) of 10-methylphenothiazine with m.p. 102-104° (m.p. 99-100°) [2].

10-Methyl-3-nitrophenothiazine and 10-methyl-3-nitro-5-oxophenothiazine. Thirty grams of 10-methylphenothiazine was dissolved with heating in 750 ml of acetic acid, and then the solution was cooled rapidly with constant stirring in cold water. A mixture of 30 ml of nitric acid (d 1.4) and 120 ml of acetic acid was added in drops to the slurry obtained on stirring and cooling at such a rate that the temperature remained below 25°; then the mixture was stirred for 1 hr and allowed to stand at room temperature. After two days, the liquid was poured into 6 liters of water, and then made neutral by the addition of powdered sodium carbonate (about 900 g); the precipitate, a mixture of a yellow powder and semisolid brown lumps, was suction-filtered, washed with water, and air-dried. Weight 36-38 g. Recrystallization of the lumps from benzene gave yellow crystals with m.p. 119-120°. The melting point given in the literature for 10-methyl-3-nitrophenothiazine is 119-121° [11]. The yellow powder melts at 170° and is much more difficultly soluble in benzene; after recrystallization from benzene it has m.p. 179-179.5°. The melting point given in the literature for 10-methyl-3-nitro-5-oxophenothiazine is 176-177° [16].

Found %: N 10.30, 10.53. $C_{13}H_{10}N_2SO_3$. Calculated %: N 10.22.

10-Methyl-3-aminophenothiazine (I). A solution of 104 g of $SnCl_4 \cdot 2H_2O$ in 240 ml of water, 120 ml of concentrated hydrochloric acid, and several pieces of metallic tin were added to 20 g of the mixed nitro compounds, after which the mixture was heated on the boiling water bath with stirring for 10-12 hr. The obtained precipitate was suction-filtered, mixed with 500 ml of distilled water, followed by the addition of 30-40 ml of 20% NaOH solution, and then the whole was extracted 6-9 times with a total of 3 liters of ether. The extract was dried over fused magnesium sulfate and filtered, and the filtrate was saturated with dry hydrogen chloride. The precipitate was suction-filtered, washed with ether, and dried in a desiccator. We obtained 10-15 g of 10-methyl-3-aminophenothiazine hydrochloride. The hydrochloride was recrystallized from alcohol by precipitation with ether to give a nearly white powder with a grayish or grayish-green tinge. M.p. 238°.

Found %: C 58.28, 58.21; H 5.08, 5.18; N 10.61, 10.64. $C_{13}H_{13}N_2S \cdot Cl$. Calculated %: C 58.97; H 4.95; N 10.58.

A portion of the ether solution of the free base obtained from the reduction of the mixed nitro compounds was evaporated to dryness, the residue dissolved in alcohol, the solution treated with activated carbon, and the filtrate diluted with water to precipitate the free 10-methyl-3-aminophenothiazine. Recrystallization from aqueous alcohol (water was added until turbidity appeared) gave the 10-methyl-3-aminophenothiazine as a white crystalline compound with m.p. 133-134°.

Found %: C 68.10, 68.03; H 5.45, 5.50. $C_{13}H_{12}N_2S$. Calculated %: C 68.38; H 5.30.

Acetyl derivatives of 10-methyl-3-aminophenothiazine. A mixture of 1 g of 10-methyl-3-aminophenothiazine hydrochloride and 5 ml of acetic anhydride was heated under reflux with a free flame for 2 hr. The mixture was then cooled somewhat and treated in drops with 15-20 ml of distilled water; the thick, oily material that separated here turned to a solid when triturated with ether. After recrystallization from alcohol, the 10-methyl-3-acetamidophenothiazine was obtained with m.p. 173-174°. Kehrmann [8] gives a melting point of 169°. Recrystallization of the crude substance from dilute acetic acid (1:2) gave a nearly white compound with m.p. 125-127°, depressing the melting point when mixed with 10-methyl-3-acetamidophenothiazine (mixed m.p. 115-118°); from its analysis it was 10-methyl-3-diacetamidophenothiazine.

Found %: N 9.26. $C_{17}H_{16}O_2N_2S$. Calculated %: N 8.97.

10-Methyl-3-benzylideneaminophenothiazine. Five grams of 10-methyl-3-aminophenothiazine hydrochloride was mixed with 50 ml of water, and then 20% NaOH solution was added until the mixture was strongly alkaline. Then the mixture was extracted several times with ether (a total of 500-600 ml). The ether solution of the free base was then treated with 2 g of freshly distilled benzaldehyde, after which the mixture was stirred for 10-15 min, and this was followed by washing first with 2% acetic acid and then with 2% sodium bicarbonate solution (100 ml each). The organic layer was dried over fused sodium sulfate, and the ether was removed by distillation, at the end under vacuum. After drying in a desiccator, the yellow residue (5.6 g) was recrystallized from alcohol in the presence of activated carbon. The 10-methyl-3-benzylideneaminophenothiazine was obtained as bright-yellow needle crystals that collected in spherical formations. M.p. 131-132°.

Found %: C 76.20, 76.00; H 5.30, 5.35; N 8.42, 8.56. $C_{20}H_{15}N_2S$. Calculated %: C 75.91; H 5.10; N 8.86.

SUMMARY

10-Methyl-3-aminophenothiazine was synthesized, and then it was characterized as the free base, and as the hydrochloride, acetyl, diacetyl, and benzylidene derivatives.

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THE REACTION OF 2,4-DINITROPHENOL WITH THIOUREA

A. F. Bogoyavlenskii and L. N. Senina

Kazan Aviation Institute

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The system 2,4-dinitrophenol-thiourea represents definite interest for the reason that, on the one hand, it can be encountered in the synthesis of explosives [1], dyes [2], and plastics [3], and, on the other, in the investigation of processes for protecting metals from corrosion (the thiourea as an inhibitor, and the dinitrophenol as an activator for the acid etching of alloys [4]). According to Kym [5], 2,4-dinitroaniline is formed when 2,4-dinitrophenol is heated with urea. The reaction of the dinitrophenol with thiourea is not reported in the literature. Below we give some data on the thermal analysis of the system 2,4-dinitrophenol-thiourea.

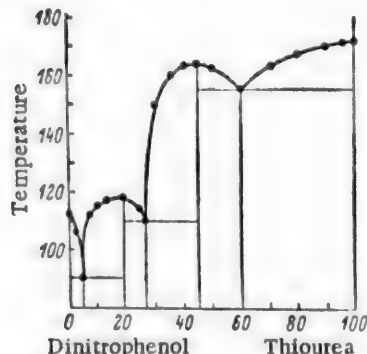


Fig. 1. Fusion diagram of the system 2,4-dinitrophenol-thiourea.

Two recrystallizations of technical 2,4-dinitrophenol from acetone gave the compound as rhombic prisms with m.p. 113°, which is in agreement with the literature data [1]. The thiourea (analytical grade) after two recrystallizations from alcohol had m.p. 172° (from the literature [6]: 180°). The melting points of the studied system were determined visually by the capillary method, using an air baffle.

The obtained data are shown on the fusion curve (Fig. 1), from which it follows that two chemical compounds are formed in the



Fig. 2. Photomicrograph of compound $4\text{C}_6\text{H}_3(\text{NO}_2)_2\text{OH} \cdot \text{CS}(\text{NH}_2)_2$ (1:120).



Fig. 3. Photomicrograph of compound $\text{C}_6\text{H}_3(\text{NO}_2)_2\text{OH} \cdot \text{CS}(\text{NH}_2)_2$ (1:120).



Fig. 4. Photomicrograph of solidified thiourea (1:120).

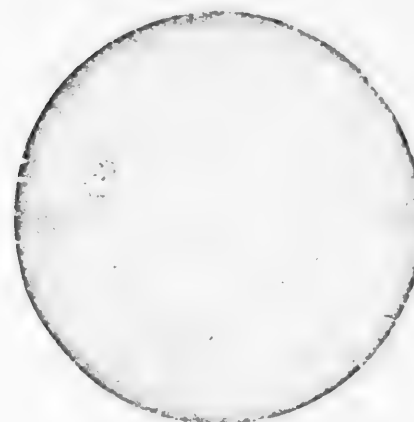


Fig. 5. Photomicrograph of solidified 2,4-dinitrophenol (1:120).

system 2,4-dinitrophenol–thiourea: one of composition $\text{C}_6\text{H}_3(\text{NO}_2)_2\text{OH} \cdot \text{CS}(\text{NH}_2)_2$ (m.p. 165°), and the other of composition $4\text{C}_6\text{H}_3(\text{NO}_2)_2\text{OH} \cdot \text{CS}(\text{NH}_2)_2$ (m.p. 118°). The three eutectic mixtures have m.p. 90, 110, and 155° , respectively.

Both of the chemical compounds belong to the berthollide type, and are characterized by their crystal structure and color (the first is yellow, while the second is orange). The crystal structure of the two compounds is shown in Figs. 2 and 3. Chemical compound $4\text{C}_6\text{H}_3(\text{NO}_2)_2\text{OH} \cdot \text{CS}(\text{NH}_2)_2$ solidifies as long, orange, needle crystals, while the compound of composition $\text{C}_6\text{H}_3(\text{NO}_2)_2\text{OH} \cdot \text{CS}(\text{NH}_2)_2$ solidifies as exceedingly fine crystalline formations with a yellow color. For comparison, the photomicrographs of thiourea and 2,4-dinitrophenol are shown in Figs. 4 and 5.

The evolution of gases, indicating the possible formation of dinitroaniline when 2,4-dinitrophenol is fused with thiourea, was not observed during the time of the experiments.

SUMMARY

1. The fusion diagram of the system 2,4-dinitrophenol–thiourea was obtained employing the visual-capillary method.

2. It was established that two chemical compounds of the berthollide type (complex addition products) are formed. These compounds have the composition $C_6H_3(NO_2)_2OH \cdot CS(NH_2)_2$ and $4C_6H_3(NO_2)_2OH \cdot CS(NH_2)_2$. It was shown that the microstructures of the two compounds are different.

3. The formation of dinitroaniline, which is formed when the dinitrophenol is reacted with urea, was not observed when 2,4-dinitrophenol is fused with thiourea.

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CONDENSATION OF o-DIAMINO DERIVATIVES OF 2-METHYLBENZOTHAZOLE WITH α -DICARBONYL COMPOUNDS

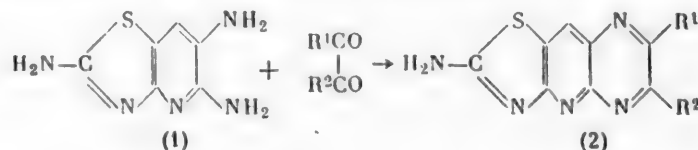
I. THIAZOLOQUINOXALINES

S. G. Fridman

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR
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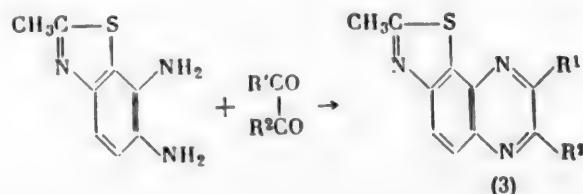
Original article submitted April 20, 1959

In a previous paper [1] we described the condensation of 2,5,6-triaminopyrido(2,3-d)thiazole (1) with α -dicarbonyl compounds, resulting in the formation of pyrazinopyridothiazole (2) derivatives.

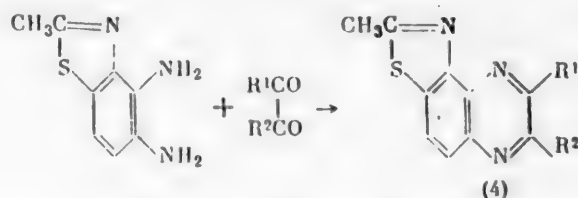


In the present paper, our objective was to synthesize some derivatives of thiazoloquinoxaline, which differs structurally from the pyrazinopyridothiazole in that the pyridine ring in the latter is replaced by the benzene ring. Condensation of the isomeric o-diamino derivatives of 2-methylbenzothiazole with α -dicarbonyl compounds gave us the three isomeric methylthiazoloquinoxalines (3), (4), and (5). Thiazoloquinoxalines of this type have remained unknown up to now.

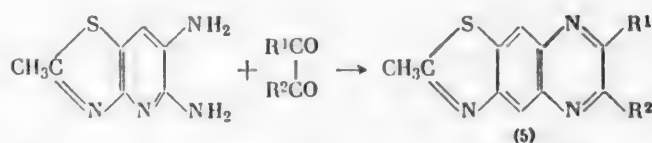
The condensation of 2-methyl-6,7-diaminobenzothiazole with α -dicarbonyl compounds yields derivatives of the angular thiazolo(4,5-h)quinoxaline.



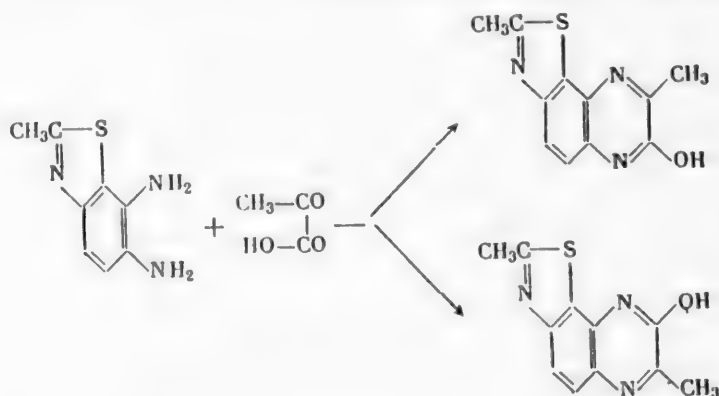
The condensation of 2-methyl-4,5-diaminobenzothiazole with α -dicarbonyl compounds yields derivatives of the second angular isomer, namely, of thiazolo(5,4-h)quinoxaline.



The condensation of 2-methyl-6,7-diaminobenzothiazole with α -dicarbonyl compounds yields derivatives of the linear isomer, namely, of thiazolo(4,5-g)quinoxaline.



The condensation of *o*-diamino derivatives of 2-methylbenzothiazole with symmetrical α -dicarbonyl compounds leads to the formation of thiazoloquinoxalines whose structure is not in doubt. The formation of two isomers is possible when the condensation is run with unsymmetrical α -dicarbonyl compounds.



We have as yet been unable to separate the products of the condensation of the *o*-diamino derivatives of 2-methylbenzothiazole with phenylglyoxal and pyrotartaric acid into the individual isomers.

Of the starting *o*-diamino derivatives of 2-methylbenzothiazole, only 2-methyl-6,7-diaminobenzothiazole is known. This compound was obtained by E. D. Sych from 2-methyl-6-chloro-7-nitrobenzothiazole by heating the compound with alcoholic ammonia solution in sealed tubes, and subsequent reduction of the obtained 2-methyl-6-amino-7-nitrobenzothiazole. The 2-methyl-6,7-diaminobenzothiazole had m.p. 184°, while its condensation product with phenanthrenequinone melted at 282°.

The nitration of 2-methyl-6-acetamidobenzothiazole gave us the known 2-methyl-6-acetamido-7-nitrobenzothiazole [2], which on hydrolysis and subsequent reduction gave us 2-methyl-6,7-diaminobenzothiazole, with the above-indicated melting point. The condensation product of this diamine with phenanthrenequinone melted at 282°.

2-Methyl-4,5-diaminobenzothiazole and 2-methyl-5,6-diaminobenzothiazole are not reported in the literature. We obtained them by the reduction of 2-methyl-4-nitro- and 2-methyl-6-nitro-5-aminobenzothiazole, respectively. These two nitro-amino derivatives of 2-methylbenzothiazole are known, and were obtained by the nitration of 2-methyl-5-acetamidobenzothiazole [3]. We made some slight modifications in the procedure used to separate the isomers obtained in the nitration, which made it possible for us to acquire a substantial amount of the starting materials.

TABLE 1

No. of compound	R'	R''	Yield (%)	Melting point	Empirical formula	Analysis results (in %)			
						found		calc.	
						N	S	N	S

Thiazolo(4,5-h)quinoxalines

I	H	H	75	137°	C ₁₀ H ₇ N ₃ S	20.86, 21.05	16.22, 16.29	20.89	15.92
II	CH ₃	CH ₃	49	145	C ₁₁ H ₁₁ N ₃ S	18.11, 18.01	14.00, 13.89	18.34	13.97
III	C ₆ H ₅	C ₆ H ₅	80	212	C ₂₂ H ₁₃ N ₃ S	11.80, 11.92	9.24, 8.97	11.89	9.06
IV	OH	OH	66	380	C ₁₀ H ₇ O ₂ N ₃ S		13.62, 13.91		13.72
V	C ₆ H ₅	H	59	212	C ₁₆ H ₁₁ N ₃ S	14.93, 14.83	11.54, 11.57	15.16	11.55
VI	CH ₃	OH	77	296	C ₁₁ H ₉ ON ₃ S	18.10, 17.96	13.88, 13.62	18.18	13.85
VII			61	294	C ₂₁ H ₁₁ N ₃ S	—	9.76, 9.77	—	9.84
VIII			67	282	C ₂₇ H ₁₉ N ₃ S	—	8.91, 9.12	—	9.11

Thiazolo(5,4-h)quinoxalines

IX	H	H	75	163	C ₁₀ H ₇ N ₃ S	20.66, 20.69	15.84, 15.64	20.89	15.92
X	CH ₃	CH ₃	54	204	C ₁₁ H ₁₁ N ₃ S	—	13.86, 13.68	—	13.97
XI	C ₆ H ₅	C ₆ H ₅	68	215	C ₂₁ H ₁₃ N ₃ S	—	8.78, 8.96	—	9.06
XII	OH	OH	64	300	C ₁₀ H ₇ O ₂ N ₃ S	—	13.74, 13.89	—	13.73
XIII	C ₆ H ₅	H	45	267	C ₁₆ H ₁₁ N ₃ S · H ₂ O	—	10.91, 10.83	—	10.84
XIV	CH ₃	OH	77	303	C ₁₁ H ₉ ON ₃ S	—	13.60, 13.62	—	13.85
XV			78	270	C ₂₀ H ₁₁ N ₃ S	12.69, 12.85	—	12.92	—
XVI			74	285	C ₂₇ H ₁₉ N ₃ S	—	—	8.81, 8.92	9.11

TABLE 1 (continued)

No. of compound	R ¹	R ²	Yield (%)	Melting point	Empirical formula	Analysis results (in %)			
						found		calc.	
						N	S	N	S

Thiazolo(4,5-g)quinoxalines

XVII	H	H	45	131	C ₁₀ H ₇ N ₃ S	20.61, 20.61	15.66, 15.81	20.89	15.92
XVIII	CH ₃	CH ₃	47	197	C ₁₂ H ₁₁ N ₃ S·H ₂ O	16.70, 16.79	12.76, 12.79	17.00	12.98
XIX	C ₆ H ₅	C ₆ H ₅	77	190	C ₂₂ H ₁₅ N ₃ S	11.87, 11.85	9.06, 8.95	11.89	9.06
XX	OH	OH	70	300	C ₁₀ H ₇ O ₂ N ₃ S	—	13.74, 13.80	—	13.73
XXI	C ₆ H ₅	H	30	207	C ₁₇ H ₁₁ N ₃ S	—	11.22, 11.34	—	11.55
XXII	CH ₃	OH	70	304--305	C ₁₁ H ₉ ON ₃ S	18.15, 18.17	13.94, 13.82	18.18	13.85
XXIII			70	289 (dec.)	C ₂₀ H ₁₁ N ₃ S	—	9.82, 9.80	—	9.84
XXIV			77	275	C ₂₇ H ₁₅ N ₃ S	11.69, 11.74	9.20, 9.36	11.96	9.11

TABLE 2

No. of compound	λ_{\max} (m μ)	log ϵ
(I)	266, 330	4.54, 3.81
(IX)	256, 324	4.42, 3.86
(XVII)	260, 336	4.40, 3.96

The α -dicarbonyl compounds used by us included: glyoxal (as the bisulfite derivative), diacetyl, benzil, phenylglyoxal, pyrotartaric acid, oxalic acid, phenanthrenequinone, and acenaphthenequinone.

The condensation of the α -diamino derivatives of 2-methylbenzothiazole with the bisulfite compound of glyoxal goes best under the conditions used to obtain the unsubstituted quinoxaline [4]. The condensation with diacetyl and with benzil was run in

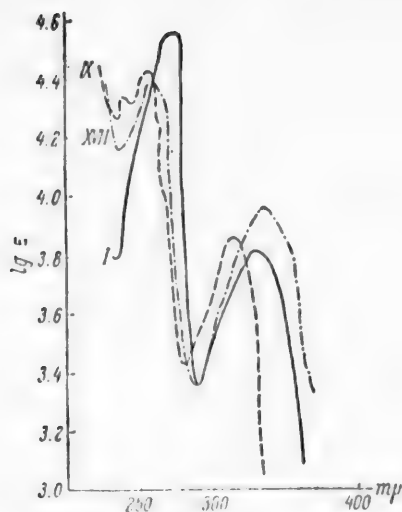
either alcohol or aqueous alcohol medium with heating on the water bath; the condensation with phenylglyoxal and with pyrotartaric acid was run in a similar manner. With oxalic acid the condensation was run in 15% hydrochloric acid, while with acenaphthenequinone and with phenanthrenequinone it was run in glacial acetic acid.

The obtained thiazoloquinoxalines are listed in Table 1. They are all crystalline compounds with melting points above 100°. Adding the thiazole ring to the quinoxaline molecule causes a substantial increase in the melting points. Thus, quinoxaline melts at 30–31°, while the thiazoloquinoxaline isomers corresponding to (I), (IX), and (XVII) have m.p. 137, 163, and 131°, respectively.

The thiazoloquinoxalines are readily soluble in alcohol, benzene, toluene, chloroform, acetic acid, and dilute mineral acids, and are difficultly soluble in water, with the exception of the unsubstituted thiazoloquinoxalines (I), (IX), and (XVII).

The 2,3-dihydroxythiazoloquinoxalines (IV), (XII), and (XX) are difficultly soluble in organic solvents, and are readily soluble in dilute aqueous alkali solutions. The thiazoloquinoxaline derivatives are less soluble than the quinoxaline derivatives; thus, 2,3-dihydroxyquinoxaline is soluble in hot water and in boiling methyl alcohol, while the 2,3-dihydroxythiazoloquinoxalines (IV), (XII), and (XX) are insoluble in hot water and very slightly soluble in boiling methyl alcohol.

Similar to the quinoxalines, the thiazoloquinoxalines form colored solutions with concentrated sulfuric acid, and are stable to dilute mineral acids and alkalis. With hydrochloric acid, the thiazoloquinoxalines form



Absorption spectra of thiazoloquinoxalines (I), (IX), and (XVII).

monohydrochlorides, with sulfuric acid they form sulfates, and with picric acid they form monopicates.

The ultraviolet absorption spectra of the thiazoloquinoxalines were taken. The absorption maxima of the thiazoloquinoxalines not substituted in the pyrazine ring are given in Table 2. The absorption curves of these compounds are shown in the figure. The measurements were made in alcohol solution using an SF-4 spectrophotometer.

EXPERIMENTAL

2-Methyl-6-aminobenzothiazole and its acetyl derivative were obtained by the improved method of I. K. Ushenko [5].

The nitration of 2-methyl-6-acetamidobenzothiazole was run under the conditions described in the literature [2], but the method used to hydrolyze the obtained nitro-acetamido derivative was changed: Dilute hydrochloric acid was used instead of alkali for the hydrolysis. To 67 g of 2-methyl-6-acetamido-7-nitrobenzothiazole, m.p. 201-202°, was added 200 ml of hydrochloric acid (1:1), and the mixture was heated on the boiling water bath for 1 hr, after which it was cooled and neutralized with ammonia. The obtained orange precipitate of 2-methyl-6-amino-7-nitrobenzothiazole was filtered, washed well with water, and dried. Weight 55 g, m.p. 253°. After recrystallization from alcohol, m.p. 253° (literature data: m.p. 250-251°).

2-Methyl-6,7-diaminobenzothiazole. To a suspension of 37 g of 2-methyl-6-amino-7-nitrobenzothiazole in 350 ml of concentrated hydrochloric acid was added, with mechanical stirring, 40 g of spongy tin in 2.5 hr, with heating on the water bath (75-80°). When all of the tin had been added, the reaction mixture was stirred for another 3 hr at the same temperature, and then allowed to stand overnight. The mixture was then diluted with 200 ml of water, after which it was heated on the water bath until all of the tin salt had dissolved, and then the solution was filtered, cooled, and made alkaline with 40% NaOH solution. The obtained light-gray precipitate of the diamine was filtered, washed with 50 ml of ice-cold water, and dried at 60°. The precipitate was extracted with boiling alcohol (500 ml), and removal of the alcohol by distillation left 23.5 g of crude 2-methyl-6,7-diaminobenzothiazole. The compound was purified by dissolving in 350 ml of alcohol, after which the solution was treated with activated carbon, filtered, and 150 ml of alcohol was distilled from the filtrate. The alcohol solution on cooling deposited 19.7 g of nearly colorless needle crystals with m.p. 184°. Further evaporation of the mother liquor gave an additional 1.5 g of the diamine, or a total of 21.7 g (70%).

2-Methyl-4,5-diaminobenzothiazole and 2-methyl-5,6-diaminobenzothiazole. 2-Methyl-5-aminobenzothiazole and its acetyl derivative were obtained by the method described in the literature [6]. The nitration of 2-methyl-5-acetamidobenzothiazole was run under the conditions described by Sych and Tolmachev [3]. The isomers obtained in the nitration, namely 2-methyl-4-nitro-5-acetamidobenzothiazole and 2-methyl-6-nitro-5-acetamidobenzothiazole, were separated by the indicated authors using the technique of fractional crystallization from alcohol and benzene. We separated the isomers obtained in the nitration of 2-methyl-5-acetamidobenzothiazole in the following manner: The precipitate obtained from the nitration of 120 g of the acetyl derivative was dissolved in 2 liters of chloroform by heating under reflux. The obtained solution was filtered from a small amount of undissolved product (5 g). The filtrate, on standing, deposited 52 g of pale-yellow needle crystals with m.p. 177-178°, which proved to be nearly pure 2-methyl-4-nitro-5-acetamidobenzothiazole. The filtrate was concentrated to a volume of 300 ml. The residual solution, on standing, deposited another 30 g of substance with m.p. 173-174°. One recrystallization from chloroform gave the pure 2-methyl-4-nitro-5-acetamidobenzothiazole with m.p. 179-180°. The chloroform filtrate from the removal of the crystalline precipitate was evaporated to dryness. The dry residue was refluxed with 250 ml of methanol for 15 min, and then filtered hot. The insoluble orange-yellow precipitate was washed with 50 ml of hot methanol and then dried. Weight 20 g, m.p. 220°. This material is pure 2-methyl-6-nitro-5-acetamidobenzothiazole. The methanol was distilled from the alcohol solution and the residue was recrystallized from chloroform to give 5 g of 2-methyl-4-nitro-5-acetamidobenzothiazole with m.p. 173-174°. As a result, the nitration of 120 g of 2-methyl-5-acetamidobenzothiazole

enabled us to obtain 87 g of 2-methyl-4-nitro-5-acetamidobenzothiazole and 20 g of 2-methyl-6-nitro-5-acetamidobenzothiazole.

The hydrolysis of 2-methyl-4-nitro-5-acetamidobenzothiazole was accomplished by heating with 1:1 HCl. From 41 g of the acetyl derivative we obtained, after recrystallization from methyl alcohol, 30.8 g (88%) of pure 2-methyl-4-nitro-5-aminobenzothiazole with m.p. 190°.

In a similar manner we isolated 15.5 g of 2-methyl-6-nitro-5-aminobenzothiazole, with m.p. 222°, from 20 g of 2-methyl-6-nitro-5-acetamidobenzothiazole.

Reduction of 2-methyl-4-nitro-5-aminobenzothiazole. The reduction was run under the conditions used to reduce 2-methyl-7-nitro-6-aminobenzothiazole. From 30 g of 2-methyl-4-nitro-5-aminobenzothiazole, after recrystallization from toluene, we obtained 20.5 g (79%) of colorless needles with m.p. 142°.

Found %: S 17.92, 17.86. $C_8H_9N_3S$. Calculated %: S 17.87.

The reduction of 2-methyl-6-nitro-5-aminobenzothiazole was run in a similar manner. From 16 g of the nitro derivative we isolated a white precipitate, which quickly darkened in the air. The precipitate was extracted with methyl alcohol, the alcohol was distilled off, and the residue was recrystallized twice from toluene. Weight 6.9 g (51%). The compound was obtained as nearly colorless needles with m.p. 163-164°.

Found %: N 23.58, 23.69; S 17.59, 17.75. $C_8H_9N_3S$. Calculated %: N 23.46; S 17.87.

8-Methylthiazolo(4,5-h)quinoxaline (I). A solution of 0.7 g of 2-methyl-6,7-diaminobenzothiazole in 10 ml of alcohol was added to a solution of 1.4 g of the bisulfite compound of glyoxal in 10 ml of water. The mixture was refluxed for 2 hr, and then filtered. The filtrate, on cooling, deposited 0.52 g of colorless crystals, which were recrystallized from aqueous alcohol (1:1); m.p. 137°.

The hydrochloride of 8-methylthiazolo(4,5-h)quinoxaline was obtained by mixing a solution of the free base in absolute alcohol with an ether solution of hydrogen chloride. The obtained precipitate was filtered, washed with ether, and dried in a vacuum-desiccator. The compound darkens at 160°, then shrivels, and melts at 240 to 243°.

Found %: Cl 14.74, 14.64. $C_{10}H_7N_3S \cdot HCl$. Calculated %: Cl 14.94.

The sulfate of 8-methylthiazolo(4,5-h)quinoxaline was obtained by adding several drops of concentrated sulfuric acid to a solution of the free base in dry ether. This resulted in the precipitation of the sulfate, which was recrystallized from anhydrous alcohol. The compound was obtained as pale-yellow nodules that darkened at 125°, and melted with decomposition at 143°.

Found %: S 19.76, 19.79. $C_{10}H_7N_3S \cdot H_2SO_4 \cdot H_2O$. Calculated %: S 20.18.

The picrate was obtained by mixing an alcohol solution of the free base with an alcohol solution of picric acid. Pale yellow needles (from alcohol) with m.p. 173°.

Found %: N 19.74, 19.76; S 7.63, 7.75. $C_{10}H_7N_3S \cdot C_6H_2OH(NO_2)_3$. Calculated %: N 19.53; S 7.44.

8-Methylthiazolo(5,4-h)quinoxaline (IX). A solution of 0.7 g of 2-methyl-4,5-diaminobenzothiazole in 20 ml of 2M acetic acid solution was added to 10 ml of a 4M sodium acetate solution, after which the mixture was heated to 60°, and then with stirring was added to a solution of 1.4 g of the bisulfite compound of glyoxal in 10 ml of water, also warmed to 60°. The yellow solution obtained in this manner was stirred at 60° for 1 hr, then cooled to 10°; 0.6 g of NaOH (as pellets) was added, and after the caustic had dissolved, 2.5 g of potassium carbonate was added. The obtained thiazoloquinoxaline was isolated from the aqueous solution by repeated extraction with small portions of benzene (a total of 150 ml). Removal of the benzene by distillation left 0.64 g of yellow crystals with m.p. 163°. The crystals were dissolved in benzene, the solution filtered, and the solvent slowly evaporated from the filtrate; this gave 0.53 g (78%) of pale-yellow plates with m.p. 163°, and readily soluble in water, alcohol, benzene, and ether.

7-Methylthiazolo(4,5-g)quinoxaline (XVII) was obtained in a similar manner from 2-methyl-5,6-diaminobenzothiazole.

2,3,8-Trimethylthiazolo(4,5-h)quinoxaline (II). A solution of 0.7 g of 2-methyl-6,7-diaminobenzothiazole in 5 ml of alcohol was added to a solution of 0.52 g of diacetyl in 15 ml of water, and the mixture was refluxed for 2 hr. The precipitate obtained on cooling was filtered, washed with water, and recrystallized from 20 ml of aqueous alcohol (1:1). The compound was obtained as colorless silky needles, difficultly soluble in water, and readily soluble in organic solvents.

The picrate was obtained as pale-yellow needles with m.p. 179° (from alcohol).

Found %: S 7.04, 7.08. $C_{12}H_{11}N_3S \cdot C_6H_2OH(NO_2)_3$. Calculated %: S 6.98.

(X) was obtained in a similar manner from 2-methyl-4,5-diaminobenzothiazole.

The condensation of 2-methyl-5,6-diaminobenzothiazole with diacetyl under the same conditions gave a solution from which a precipitate failed to deposit. The solution was evaporated to dryness, and the dry residue was extracted with benzene. The obtained 2,3,7-trimethylthiazolo(4,5-g)quinoxaline (XVIII) was recrystallized from a mixture of benzene and alcohol. Pale-yellow needles, soluble in water and in organic solvents. The compound forms a stable monocrystalhydrate.

The picrate was obtained as yellow needles with m.p. 196° (from alcohol).

Found %: S 7.04, 7.19. $C_{18}H_{14}O_7N_6S$. Calculated %: S 6.98.

8-Methyl-2,3-diphenylthiazolo(4,5-h)quinoxaline (III). A mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole and 0.84 g of benzil in 25 ml of alcohol was refluxed for 30 min. A yellow crystalline precipitate began to deposit within 5 min after the start of reflux. This precipitate was filtered, washed with alcohol, and recrystallized from benzene. The compound was obtained as light-yellow prisms, insoluble in water, difficultly soluble in alcohol and acetone, and readily soluble in benzene, toluene, acetic acid, and dilute hydrochloric acid.

2,3-Diphenyl-8-methylthiazolo(5,4-h)quinoxaline (XI) was obtained in a similar manner from 2-methyl-4,5-diaminobenzothiazole; pale-yellow needles (from benzene).

2,3-Diphenyl-8-methylthiazolo(4,5-g)quinoxaline (XIX) was obtained from 2-methyl-5,6-diaminobenzothiazole, and was recrystallized from 90% alcohol. The compound is difficultly soluble in water, readily soluble in alcohol and acetone, and much more soluble in benzene and toluene than isomers (III) and (XI).

2,3-Dihydroxy-7-methylthiazolo(4,5-h)quinoxaline (IV). A mixture of 0.7 g of 2-methyl-6,7-diaminobenzothiazole, 0.54 g of oxalic acid, and 15 ml of 15% hydrochloric acid was refluxed for 1 hr. A white crystalline precipitate gradually deposited from the solution; it was filtered, washed with water, and then with alcohol and with ether. The compound is almost insoluble in water and is difficultly soluble in organic solvents, but is readily soluble in dilute alkalis and aqueous sodium carbonate solution. The precipitate was purified by dissolving in 2% sodium bicarbonate solution, followed by treatment with activated carbon, after which the solution was filtered, and the filtrate was acidified with acetic acid. Here we obtained 0.6 g of colorless microscopic needles, which failed to melt up to 330°.

2,3-Dihydroxy-7-methylthiazolo(5,4-h)quinoxaline (XII) was obtained from 2-methyl-4,5-diaminobenzothiazole, while 2,3-dihydroxy-6-methylthiazolo(4,5-g)quinoxaline (XX) was obtained from 2-methyl-5,6-diaminobenzothiazole in a similar manner.

2(3)-Phenyl-7-methylthiazolo(4,5-h)quinoxaline (V). A hot solution of 0.7 g of 2-methyl-6,7-diaminobenzothiazole in 10 ml of methanol was added to a hot solution of 0.54 g of phenylglyoxal in 10 ml of methanol. The obtained solution immediately turned yellow, and yellow needles began to separate from solution after 5 min heating on the boiling water bath. After 1 hr, the crystals were filtered and washed with alcohol and ether; m.p. 210°. After one recrystallization from alcohol or benzene, m.p. 212°. Further recrystallization failed to raise the melting point. The compound is difficultly soluble in water, more soluble in alcohol, and readily soluble in benzene, toluene, chloroform, acetic acid, and dilute hydrochloric acid.

To separate the postulated isomers, the compound after isolation from the reaction mixture was dissolved in chloroform, and the chloroform solution was passed through a chromatographic column filled with aluminum oxide. One zone was obtained, which was eluted with chloroform. Removal of the solvent by distillation left a white precipitate with m.p. 212°, which was not raised by recrystallization from alcohol or benzene. We were unable to find the postulated isomers.

2(3)-Phenyl-7-methylthiazolo(5,4-h)quinoxaline (XIII) and 2(3)-phenyl-6-methylthiazolo(4,5-g)quinoxaline (XXI) were obtained in a similar manner. The last compound was recrystallized from 90% alcohol. It is much more soluble in organic solvents than the angular isomers.

2(3)-Hydroxy-3(2),8-dimethylthiazolo(4,5-h)quinoxaline (VI). A solution of 0.5 g of freshly distilled pyrotartaric acid in 2 ml of water was added to a solution of 0.7 g of 2-methyl-6,7-diaminobenzothiazole in 20 ml of 50% alcohol. The solution turned yellow immediately, and a yellow precipitate began to deposit in 5-10 min. After standing for 1 hr, the precipitate was filtered and then washed with water and with alcohol. The compound was purified by dissolving in 20 ml of 1% NaOH solution, followed by filtration of the solution and acidification of the filtrate with acetic acid. This resulted in the deposition of homogeneous pale-yellow needles, difficultly soluble in water and in organic solvents. (XIV) and (XXII) were obtained in a similar manner. In contrast to (VI) and (XIV), (XXII) is readily soluble in organic solvents. To isolate it from the reaction mixture, the solvent was removed by distillation, and the residue was recrystallized from a small amount of benzene.

The acenaphtho derivatives (VII), (XV), and (XXIII) were obtained by mixing hot solutions of the diamine in alcohol and the acenaphthenequinone in acetic acid. The compounds were recrystallized from xylene.

The phenanthrene derivatives (XVI) and (XXIV) were obtained in a similar manner, and they were recrystallized from benzene.

SUMMARY

1. The following o-diamino derivatives of 2-methylbenzothiazole were obtained: 2-methyl-4,5-diaminobenzothiazole, 2-methyl-5,6-diaminobenzothiazole, and the previously known 2-methyl-6,7-diaminobenzothiazole.

2. The following three types of isomeric thiazoloquinoxaline derivatives were synthesized by the condensation of o-diamino derivatives of 2-methylbenzothiazole with α -dicarbonyl compounds: thiazolo(4,5-h)quinoxalines, thiazolo(5,4-h)quinoxalines, and thiazolo(4,5-g)quinoxalines. The properties of these compounds were studied, and their ultraviolet absorption spectra were taken.

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CATALYTIC SYNTHESIS OF ALDEHYDES AND KETONES

VII. SYNTHESIS OF ACETALDEHYDE FROM ACETIC ACID AND FORMALDEHYDE

I. P. Yakovlev

Kostroma Textile Institute

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Earlier, we had proposed a general mechanism for the formation of aldehydes and ketones from acids, derivatives of acids, aldehydes, and their mixtures [1]. In the present investigation, undertaken for the purpose of confirming the earlier-expressed postulations, we studied the relationship between the yield of acetaldehyde and the temperature when acetic acid is reacted with formaldehyde on chromium-copper catalyst, and we also examined the kinetics of the decomposition of both the starting materials and the reaction products on the same catalyst. The rules that evolved as a result of this study make it possible to state that the earlier-proposed scheme for the formation of aldehydes and ketones from acids also applies in the present case.

The reaction of acetic acid with formaldehyde should yield acetaldehyde and formic acid in accordance with reaction (1).



Experiments revealed that the given reaction proceeds in the temperature range 180-380° (see table). A sharp increase in the amount of acetaldehyde (see Experimental), and a reduction in the amount of formic acid is observed at higher temperatures. It can be assumed that at these temperatures the formic acid begins to react with acetic acid in accordance with scheme (2).



Reaction (1) is the principal, if not the only source of the formation of formic acid under our experimental conditions. Actually, its formation fails to occur when either formaldehyde or the secondary reaction products are decomposed on the indicated catalyst. Formaldehyde decomposed with the formation of H_2 , CO , and CO_2 , in which connection the total amount of CO_2 in the gases decreases and the amounts of H_2 and CO increase with increase in the temperature. This means that at high temperatures the decomposition of formaldehyde proceeds mainly in accordance with scheme (3).



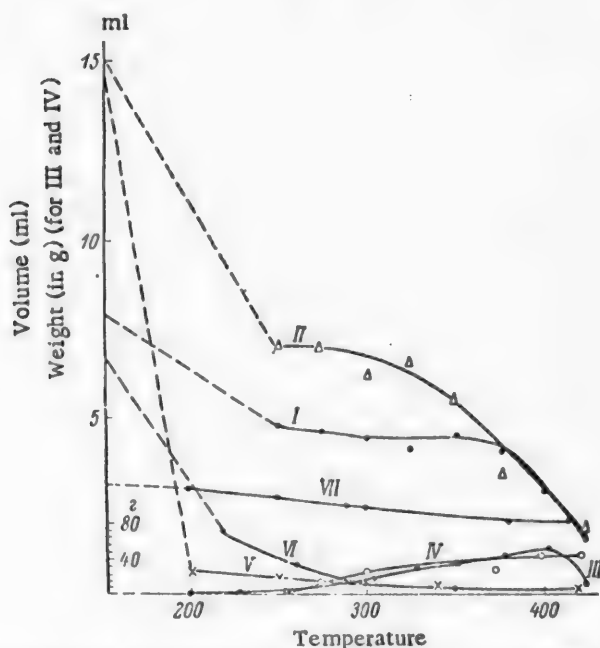
The mechanism for the formation of the CO_2 is not clear. In any case, the formation of the CO_2 is not due to the decomposition of formic acid, since this compound could not be detected in the experiment on the decomposition of formaldehyde. Also, there is no basis to assume that the CO_2 is formed due to conversion of the CO , since this conversion goes with difficulty and requires higher temperatures.

The noticeable decomposition of acetic acid in the presence of H_2 begins only at temperatures above 250°, and it goes with the formation of acetone. Formic acid and acetaldehyde are not formed. The gas contains nearly equal amounts of CO and CO_2 .

At temperatures up to 300°, the formation of acetaldehyde also goes mainly, if not exclusively, in accordance with reaction (1). It was already stated earlier that the other possible reaction for its formation, namely (2), begins to proceed at a noticeable rate only at higher temperatures.

Reaction for the Decomposition of a Mixture of Acetic Acid (95%) and Formaldehyde (34.1% Solution) (Taken in a 1:1 Mole Ratio)

Temp. °C	Total acidity in 0.5 ml of catalyzate (ml of 0.5N NaOH)	Total amt. of carbonyl comp. in 0.5 ml of catalyzate (ml of 0.5N NaOH)	Amt. of HCOOH in 1000 ml of catalyzate (in g)	Comp. of gases (in vol. %)			Yield of gas (ml/min)
				CO ₂	CO	H ₂	
0°	7.8	15.7	0	—	—	—	—
175	—	—	1.4	—	—	—	—
200	—	—	3.0	—	—	—	—
225	—	—	3.7	—	—	—	—
250	4.8	7.1	8.0	—	—	—	—
275	4.7	7.0	10.6	17.6	30.6	54.2	5
300	4.5	6.1	21.2	17.6	30.2	52.2	10
325	4.2	6.6	30.2	20.2	27.4	52.4	32
350	4.6	5.6	38.2	22.6	24.6	52.8	40
375	4.3	3.4	47.4	20.0	23.6	50.0	45
400	3.0	2.9	49.7	20.0	23.6	50.0	110
425	2.3	2.0	16.1	—	—	—	130

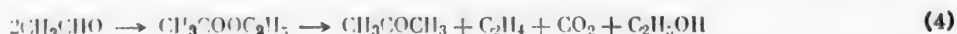


Change in the amounts of products from the reaction of acetic acid with formaldehyde on a chromium-copper catalyst as a function of the temperature. I) Total acidity (in ml of 0.1N NaOH); II) amount of carbonyl compounds (in ml of 0.5N NaOH consumed for back titration, using the hydroxylamine method); III) HCOOH (in g/1000 ml of catalyzate); IV) CH₃CHO (the same as III); V) CH₂O in the reaction for its decomposition (the same as II); VI) HCOOH in the reaction for its decomposition (in ml of 0.5N NaOH); VII) CH₃COOH (the same as VI); The dotted continuations of curves I, II, V, VI, and VII indicate the initial concentrations.

Some remarks should also be made regarding the secondary processes that take place on the indicated catalyst. Thus, acetaldehyde proved to be a quite stable compound. Its noticeable decomposition begins only at temperatures exceeding 350°. Hydrogen represents half of the gases that are formed here. At lower temperatures the amount of CO formed greatly exceeds the amount of CO₂. These amounts approach each other as the temperature is raised. The formation of acids is not observed.

Although we failed to make a special study of the decomposition processes of acetaldehyde in the present

investigation, still it is possible to assume that it does not go through the ester [2]. In case the ester was formed, it would decompose with the formation of ethylene, in accordance with scheme (4); we failed to find ethylene in the reaction gases.



It was also necessary to establish the manner in which acetone behaves under the investigated conditions. The experiments revealed that acetone begins to decompose at very high temperatures (390-420°). As a result, the decomposition of acetone fails to exert an influence on the main course of the investigated process.

Mention should also be made of the remarkable fact that the decomposition (in the presence of water) of formaldehyde, acetaldehyde, and acetone results in the formation of the three gases H_2 , CO , and CO_2 , in which connection the amount of H_2 and CO_2 increases with increase in the temperature. It is impossible to attribute this to a conversion of the carbon monoxide, since such conversion occurs only at higher temperatures. It is obvious that all of these gases are formed directly from the carbonyl compounds.

Formic acid proved to be an unstable compound. Nevertheless, its concentration keeps increasing constantly with increase in the temperature up to approximately 380-390°. Such a phenomenon can be explained only by the fact that its rate of formation exceeds its decomposition rate and, failing to decompose, it succeeds in escaping from the high-temperature zone. At low temperatures the decomposition of formic acid proceeds in accordance with scheme (5), and at higher temperatures in accordance with scheme (6).



The nature of the change in the concentrations of the carbonyl compounds and acids in the examined processes, taking place on a copper-chromium catalyst, is shown in the figure. Attention is drawn to the fact that the appearance of formic acid in the reaction products precedes the appearance of acetaldehyde, but it fails to take an active part in the formation of acetaldehyde at temperatures below 380°. A sharp decrease in its concentration is observed at higher temperatures, possibly because it begins to react in accordance with scheme (2).

The present investigation indicates that it is possible to obtain acetaldehyde from acetic acid and formaldehyde, and it substantiates the earlier-proposed scheme for the conversion of acids and aldehydes and their mixtures to other aldehydes and ketones.

EXPERIMENTAL

Preparation of catalyst. Solutions of 121.6 g of $(\text{NH}_4)_2\text{CrO}_4$ in 400 ml of water and 232.6 g of $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ in 250 ml of water were poured together, and then 60 ml of 25% NH_4OH solution was added. The precipitate was filtered and without washing was dried and calcined. Twenty grams of the catalyst was deposited on asbestos wool. The same portion of catalyst was used in all of the experiments.

Method of operation. Rheometers were used to measure the amounts of ingoing and outgoing gas. An apparatus designed by the All-Union Heat Engineering Institute was used for the gas analysis. The amounts of H_2 , CO , CO_2 , and unsaturated hydrocarbons were determined. Only those liquid reaction products were analyzed that collected in the receiver after water cooling. To determine quantitatively the yield of acetaldehyde, we used an additional trap, filled with alcohol (95%), and immersed in a cooling mixture of alcohol and dry ice. To analyze the catalyzate, the acids were neutralized with sodium carbonate and the carbonyl compounds were steam-distilled. The formic acid was determined in accordance with [3], while the carbonyl compounds were determined by the hydroxylamine method.

Colorimetric determination of acetaldehyde. For the analysis a solution was prepared by the successive pouring together of 5 ml of 4% hydroxyquinoline, 5 ml of 1.43% sodium nitroprusside, 40 ml of water, and then 1 ml of the catalyzate. The solution was analyzed colorimetrically after standing for 30 min.

The amount of acetaldehyde in 1.0 ml of catalyzate, determined colorimetrically, when a mixture of 1 mole of acetic acid and 1 mole of 29% formaldehyde solution was passed over the catalyst at a feed rate of 66 ml/hr gave the following results (in g): 0-250° 0, 275° 0.0132, 300° 0.0264, 375° 0.0308, 400° 0.0440, 425° 0.0440.

Quantitative determination of formic acid. a) After removal of the neutral products by steam-distillation, the residue was treated with 10 ml of 0.1N KMnO_4 solution on the boiling water bath for 10 min, acidified with 20 ml of 2 N H_2SO_4 , and then titrated with 0.1N oxalic acid solution.

b) One milliliter of the catalyzate was neutralized with sodium carbonate and then treated with steam as in the previous case; then the residue was acidified with 5 ml of 10% phosphoric acid (1:5), and the mixture was steam-distilled until 100 ml of distillate had been collected. The distillate was analyzed in the same manner as in a. The results are given in the table and plotted in the figure (Curve III); only the values obtained by method a were used. Method b gives values that differ from those obtained using method a by 1.0-1.5 ml of 0.1N oxalic acid.

SUMMARY

1. In principle, it was established that it is possible to obtain acetaldehyde from acetic acid and formaldehyde.
2. The earlier-expressed mechanism for the ketonization of acids, derivatives of acids, and aldehydes was confirmed on the example of acetic acid and formaldehyde.

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COMPLEXES OF TIN. V.

T. N. Sumarokova, T. V. Medvedeva, and I. G. Litvyak

Institute of Chemistry, Academy of Sciences of the Kazakh SSR

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Complexes of type $\text{SnX}_4 \cdot 2\text{A} \cdot 2\text{B}$ and $\text{SnX}_4 \cdot 2\text{A} \cdot \text{B}$ [1-5] were obtained by reacting complex acids of type $\text{SnX}_4 \cdot 2\text{RCOOH}$ with substances (oxonium bases) which, in view of their quite weak basic properties, are incapable of displacing the addenda from the inner sphere. The formation of such mixed compounds is also possible in the reaction of stronger bases with the complex acids $\text{SnX}_4 \cdot 2\text{RCOOH}$. In this case, the mixed complexes may be obtained as intermediate products in the displacement reactions. Thus, for example, Usanovich and Kalabanovskaya [6], in describing the reaction for the displacement of acetic acid from the inner sphere of the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$, expressed the opinion that the first act in the displacement reaction is the formation of the intermediate complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_5\text{N}$.

The present paper is a continuation of a series of investigations on the preparation of mixed complexes of tin halides, and has as its goal a study of the displacement of addenda from the inner sphere of compounds of type $\text{SnCl}_4 \cdot 2\text{RCOOH}$ by nitrogen-containing organic bases. A study was made of the displacement of CH_3COOH from the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ by pyridine, piperidine, and aniline. A study of complex formation in the systems $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ - organic base, and of the displacement of acid from $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ by bases, was made via the synthesis of the complexes, which were then subjected to thermal decomposition, and also by employing the cryoscopic method.

*Original Russian pagination. See C.B. translation.

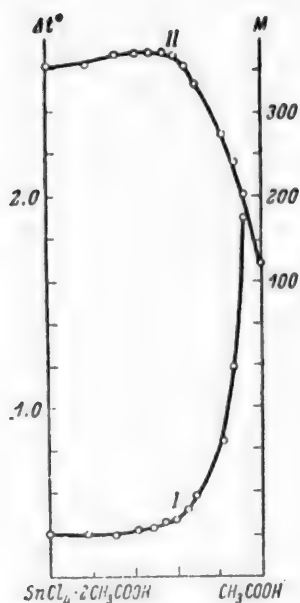


Fig. 1. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{CH}_3\text{COOH}$ (in mole %).

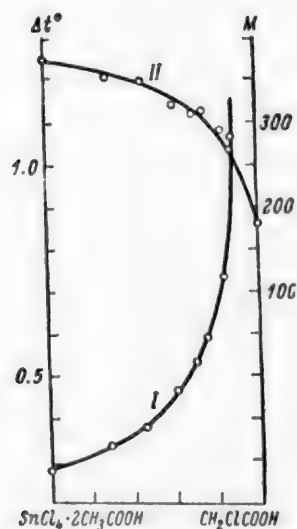


Fig. 2. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{CH}_2\text{ClCOOH}$ (in mole %).

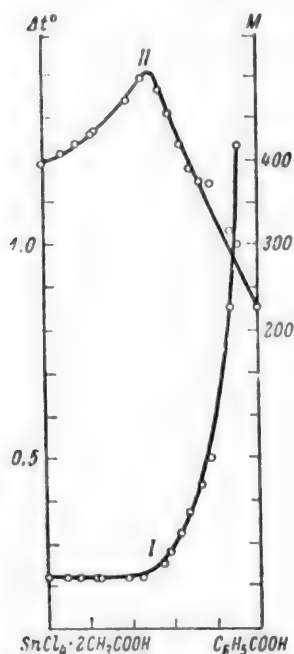


Fig. 3. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{C}_6\text{H}_5\text{COOH}$ (in mole %).

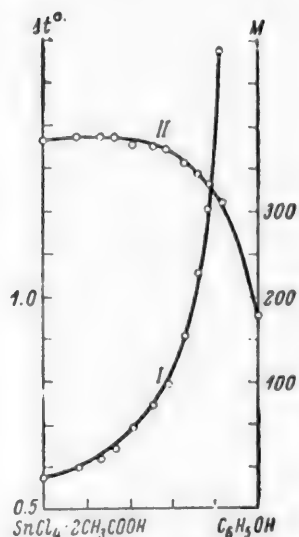


Fig. 4. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{C}_6\text{H}_5\text{OH}$ (in mole %).

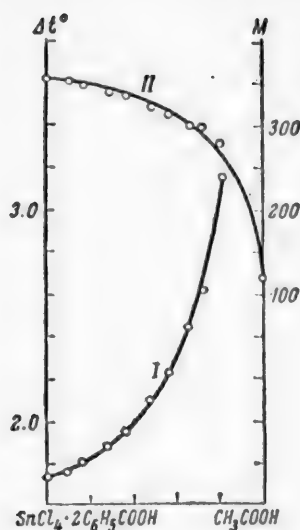


Fig. 5. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{CH}_3\text{COOH}$ (in mole %).

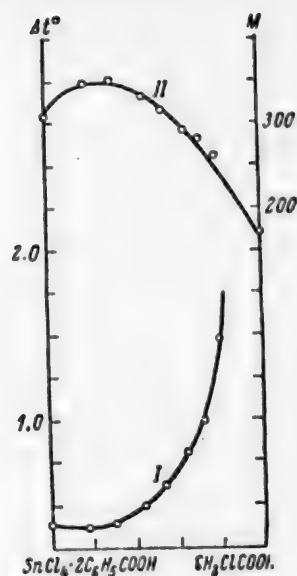


Fig. 6. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{CH}_2\text{ClCOOH}$ (in mole %).

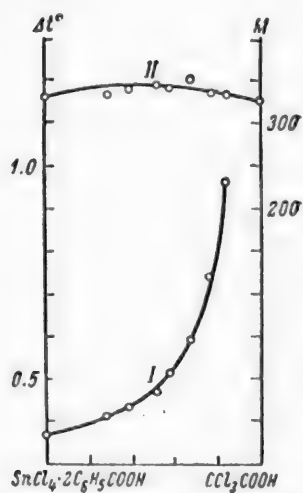


Fig. 7. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{CCl}_3\text{COOH}$ (in mole %).

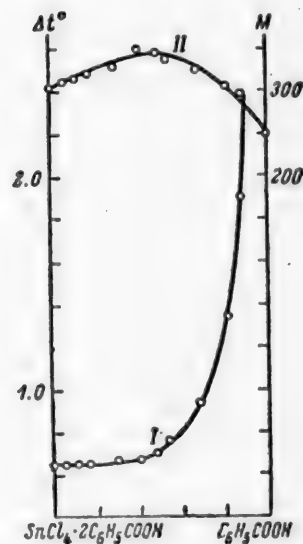


Fig. 8. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{C}_6\text{H}_5\text{COOH}$ (in mole %).

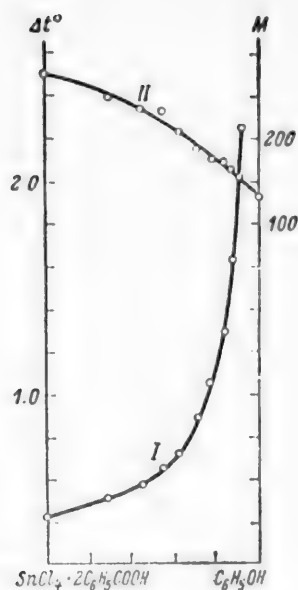


Fig. 9. Dependence of the depression (I) and molecular weight (II) on the composition of the system $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{C}_6\text{H}_5\text{OH}$ (in mole %).

or $\text{C}_6\text{H}_5\text{OH}$ is added to a solution of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ in benzene, or to a solution of $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH}$ in *p*-dichlorobenzene, the depression rises slowly at the start, and then, beginning around 50 mole %, it rises rapidly. In all cases, the curves for the dependence of the molecular weight on the composition show a positive deviation of the values from additivity. The maximum deviation in the value of the molecular weight occurs at an equimolar ratio of the components, which is linked with the formation of compounds of general formula $\text{SnCl}_4 \cdot 2\text{RCOOH} \cdot \text{B}$. The values of the molecular weights at the points corresponding to the composition of these compounds are less than the whole, and greater than one-half the formula molecular weight. This indicates that the reaction for the formation of the compounds does not go to completion.

As a result, a cryoscopic study of the systems formed by $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ and $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH}$ with oxonium bases confirmed our earlier conclusions regarding the formation of complexes of type $\text{SnCl}_4 \cdot 2\text{RCOOH} \cdot \text{B}$.

2. System $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{C}_5\text{H}_5\text{N}$. Vigorous reaction took place when benzene solutions of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ were mixed with pyridine, leading to the deposition of the formed complexes in the precipitate.

Analysis of the precipitates depositing from the mixtures gave the following results.

When the components were mixed in a 1:2 ratio:

Found %: Sn 25.87, 26.01, 26.36; Cl 30.22, 30.45, 30.58, 30.78.

When the components were mixed in a 1:1 ratio:

Found %: Sn 25.58, 25.71, 26.17; Cl 30.15. $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_5\text{N}$. Calculated %: Sn 22.02; Cl 26.32. $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_5\text{N}$. Calculated %: Sn 25.81; Cl 30.67.

The results of analyzing the precipitates obtained on mixing the components in the ratios of 1:1 and 1:2 indicate that in both cases the precipitates represent the same compound, corresponding to the formula $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_5\text{N}$. The filtrate from the 1:1 mixture had an acid reaction, while the filtrate from the 1:2 mixture had an alkaline reaction (to methyl orange). For this reason, we decided to determine the amount of unreacted pyridine by titrating the filtrate with 0.1N HCl solution (in the presence of crystal violet, picric acid, Tropaeolin 00, and thymol blue), and established that the amount of excess pyridine in the filtrate from the 1:2

EXPERIMENTAL

The preparation and purification of the compounds [1-7], and also the technique of the cryoscopic determinations [7,8] were described earlier. The constants of the compounds agreed with the literature data. The complexes were synthesized by the procedure of mixing solutions of the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ in benzene with the bases (using 1 mole of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ per mole of base and 1 mole of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ per 2 moles of base). The obtained precipitates were separated from the mother liquor on a glass filter, washed well with benzene, dried in a vacuum-desiccator over P_2O_5 , and then analyzed for tin and chlorine.

1. Systems $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{C}_6\text{H}_5\text{COOH}$, CH_3COOH , CH_2ClCOOH , $\text{C}_6\text{H}_5\text{OH}$ and $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{C}_6\text{H}_5\text{COOH}$, CH_3COOH , CH_2ClCOOH , CCl_3COOH , $\text{C}_6\text{H}_5\text{OH}$ were studied earlier on the basis of the electroconductivity, viscosity, density, and fusion [1-5]. Here the existence of complexes of the type $\text{SnCl}_4 \cdot 2\text{RCOOH} \cdot \text{B}$ was established, where B is the oxonium base molecule. In the systems $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{CCl}_3\text{COOH}$ and $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH} - \text{CCl}_3\text{COOH}$, a reaction was detected which we attributed to the formation of the hydrogen bond, since we failed to observe an increase in the electroconductivity in these systems.

Here we will present the results of a cryoscopic study of these systems, represented in the form of depression-composition and molecular weight-composition diagrams (Figs. 1-9). From the graphs it can be seen that as CH_3COOH , CH_2ClCOOH , CCl_3COOH , $\text{C}_6\text{H}_5\text{COOH}$,

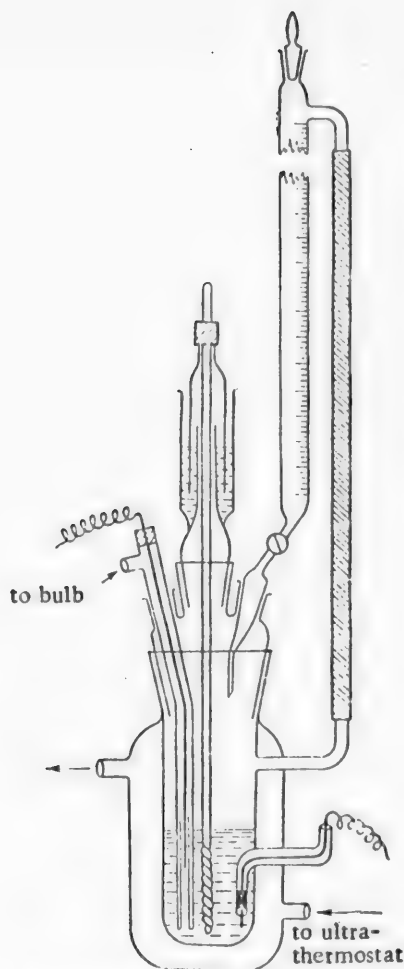


Fig. 10. Apparatus for differential potentiometric titration.

potentiometric titration was run in a special apparatus (Fig. 10), making it possible to take the differential curve.

The results of the cryoscopic titration of the complex acid with pyridine in benzene solution are shown in Fig. 11. As constantly increasing amounts of pyridine are added to the complex acid in benzene solution the depression drops at first, passes through a minimum at 50 mole%, and then rises sharply. The drop in the depression up to 50 mole% is caused by the formation of the equimolecular compound and its deposition in the precipitate.

Consequently, the results obtained in both the potentiometric and the cryoscopic titrations of the complex acid with pyridine, and also the analysis results, indicate that the complex acid adds one mole of pyridine.

The complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_5\text{N}$ is a colorless crystalline substance, relatively stable in the air, difficultly soluble in benzene and in alcohol, and readily soluble in water. First the liberation of acetic acid, and then the appearance of a sublimate was observed when the complex was heated.

Analysis of sublimate.

Found %: Sn 27.52, 26.30, 27.65, 27.30; Cl 32.06, 33.19, 33.94, 33.44, 33.60. $\text{SnCl}_4 \cdot 2\text{C}_5\text{H}_5\text{N}$.
Calculated %: Sn 28.53; Cl 33.87.

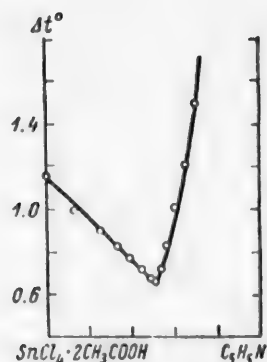


Fig. 11. Curve for the cryoscopic titration of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ with pyridine.

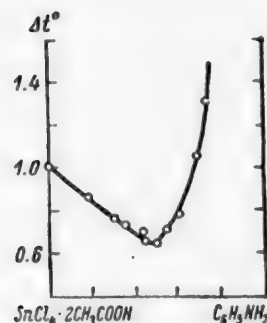


Fig. 12. Curve for the cryoscopic titration of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ with aniline.

From the analysis data it can be seen that the thermal decomposition of the complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_6\text{H}_5\text{N}$ results in the pyridine displacing the acetic acid from the inner sphere of the complex acid with the formation of the complex $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{N}$.

3. System $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{C}_6\text{H}_5\text{NH}_2$. The same as in the preceding system, the components also reacted vigorously in this case, with the evolution of heat and the formation of a precipitate. The results obtained in analyzing the precipitates are given below.

When the components were mixed in a 1:2 ratio:

Found %: Sn 25.57, 24.70, 25.65; Cl 29.19, 29.90, 30.00.

When the components were mixed in a 1:1 ratio:

Found %: Sn 24.15, 23.28, 23.20, 23.89, 23.62, 24.24, 23.68; Cl 33.73, 33.82, 33.35. $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_6\text{H}_5\text{NH}_2$. Calculated %: Sn 25.05; Cl 29.93. $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_6\text{H}_5\text{NH}_2$. Calculated %: Sn 20.93; Cl 25.97.

The analysis results indicate that the precipitate obtained from the 1:2 mixture is the complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_6\text{H}_5\text{NH}_2$, while the product obtained from the 1:1 mixture is apparently the same compound, but containing the solvolysis product $(\text{C}_6\text{H}_5\text{NH}_3)_2\text{SnCl}_6$ as impurity.

The results of the cryoscopic titration of the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ with aniline are shown in Fig. 12. From Fig. 12 it can be seen that as aniline is added to the benzene solution of the complex acid the depression drops due to the deposition of the complex in the precipitate, reaches its minimum value at 50 mole%, and then rises sharply. Such a relationship between the depression and the composition indicates the formation of the complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_6\text{H}_5\text{NH}_2$, similar to the complex with pyridine. The complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_6\text{H}_5\text{NH}_2$ is relatively stable in the air, is difficultly soluble in benzene and in alcohol, and is readily soluble in water.

The liberation of acetic acid and the formation of a sublimate were also observed when this complex was subjected to thermal decomposition. The analysis results for the sublimate are given below.

Found %: Sn 24.82, 24.68, 24.30; Cl 29.79, 30.51, 30.78. $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{NH}_2$. Calculated %: Sn 26.58; Cl 29.93.

The analysis results obtained for the sublimate indicate that the thermal decomposition of the complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_6\text{H}_5\text{NH}_2$ leads to the aniline displacing the acetic acid from the inner sphere of the complex and the formation of the compound $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{NH}_2$.

4. System $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} - \text{C}_5\text{H}_{11}\text{N}$. Reaction of the complex acid with piperidine went with the evolution of heat, and resulted in the deposition of complexes in the precipitate. The analysis results for the obtained precipitates are given below.

When the components were mixed in a 1:2 ratio:

Found %: Sn 21.71, 21.23; Cl 26.09, 26.16. $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_{11}\text{N}$. Calculated %: Sn 21.55; Cl 25.74.

When the components were mixed in a 1:1 ratio:

Found %: Sn 25.61, 25.36; Cl 30.26, 30.46, 29.59. $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_{11}\text{N}$. Calculated %: Sn 25.54; Cl 30.52.

The analysis data obtained for the precipitates indicate that the complex acid reacts with piperidine to form the complexes $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_{11}\text{N}$ and $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_{11}\text{N}$.

The results of the cryoscopic titration of the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ with piperidine are shown in Fig. 13. An examination of this graph reveals that as piperidine is added to a benzene solution of the complex, the depression drops quite rapidly at the start, then shows some retardation as the equimolecular composition

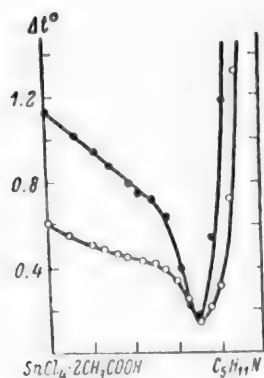


Fig. 13. Curves for the cryoscopic titration of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ with piperidine.

is approached, after which the depression again drops sharply and then, beginning with 33 mole% of the complex acid, it rises steadily. This behavior of the depression is linked with the formation of the two complexes $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_{11}\text{N}$ and $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_{11}\text{N}$, which deposit in the precipitate.

Consequently, based on the analysis data and the results of the cryoscopic titration, we came to the conclusion that the complex acid adds either one or two molecules of piperidine in the outer sphere.

The complexes $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_{11}\text{N}$ and $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_{11}\text{N}$ are crystalline compounds, difficultly soluble in organic solvents. The complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{C}_5\text{H}_{11}\text{N}$ melts with decomposition at 194° , while the complex $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{C}_5\text{H}_{11}\text{N}$ melts without decomposition at 144° , changing to an extremely viscous, clear liquid.

DISCUSSION OF RESULTS

A cryoscopic study of the reaction of the complex acids $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ and $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH}$ with oxonium bases (CH_3COOH , CH_2ClCOOH , CCl_3COOH , $\text{C}_6\text{H}_5\text{COOH}$, and $\text{C}_6\text{H}_5\text{OH}$) confirmed both the earlier-obtained data relating to the physicochemical analysis of the liquid phase of these systems and our conclusions regarding the formation of the mixed complexes $\text{SnCl}_4 \cdot 2\text{RCOOH} \cdot \text{B}$ (where B is the oxonium base molecule), in which different addenda are contained in the inner and outer spheres.

The reaction of aniline, pyridine, and piperidine with the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ gave mixed complexes, which appear as intermediate products in the reaction for the displacement of carboxylic acids from the inner sphere of the complex acid $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$. This displacement reaction once again demonstrates the fact that carboxylic acids, being amphoteric compounds, function as bases toward stannic chloride, since they are displaced by stronger organic bases (pyridine, piperidine, aniline). Here the stannic chloride functions as an acid toward these compounds.

SUMMARY

1. A cryoscopic study was made of the systems formed by the complex acids $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ and $\text{SnCl}_4 \cdot 2\text{C}_6\text{H}_5\text{COOH}$ with oxonium bases (CH_3COOH , CH_2ClCOOH , CCl_3COOH , $\text{C}_6\text{H}_5\text{COOH}$, and $\text{C}_6\text{H}_5\text{OH}$). Previous data on the formation of mixed complexes of type $\text{SnCl}_4 \cdot 2\text{RCOOH} \cdot \text{B}$ (where B is the base molecule) were confirmed.

2. The reactions for the formation of complexes between $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH}$ and pyridine, piperidine, and aniline were examined. Here the existence of complexes of type $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot \text{B}$ was established, and in the case of piperidine, also of $\text{SnCl}_4 \cdot 2\text{CH}_3\text{COOH} \cdot 2\text{B}$.

It was shown that the thermal decomposition of these complexes leads to the organic base displacing the acetic acid from the inner sphere of the complex with the formation of complexes of the type $\text{SnCl}_4 \cdot 2\text{B}$.

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COMPLEXES OF TIN AND TITANIUM HALIDES WITH ORGANIC COMPOUNDS CONTAINING C = O AND -COC- GROUPS

T. Sumarokova, Yu. Nevskaya, and É. Yarmukhamedova

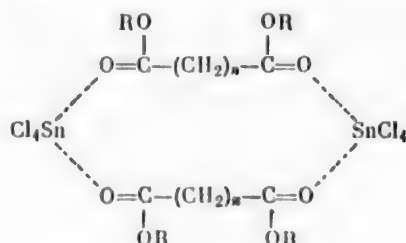
Institute of Chemistry, Academy of Sciences of the Kazakh SSR

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Complexes of stannic chloride and bromide with dicarboxylic acids and their esters of composition $\text{SnCl}_4 \cdot A$ are described in the literature [1-5]. Hieber and co-workers [3-5] came to the conclusion that these complexes have the following structure:



It is possible to assume that not only dicarboxylic acids and their esters but also other organic compounds containing two C = O or -COC- groups are capable of giving complexes with a dimeric structure when reacted with tin and titanium halides. In connection with such an assumption, we decided to reinvestigate the reaction of titanium and tin halides with quinone, dioxane, 2-furaldehyde, and diethyl oxalate.

The reaction of stannic chloride with quinone was studied by K. Meyer [6]; he isolated a complex compound from the benzene solutions, to which he assigned the composition $\text{SnCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2 \cdot \text{C}_6\text{H}_6$. Such a composition for the compound does not seem very probable to us for the following reasons. It is known that stannic chloride does not react with benzene [7], but readily reacts with quinone, the latter being an oxygen-containing compound with definite basic properties. For this reason it is difficult to see benzene adding to stannic chloride in the presence of excess quinone. We postulated that the complex of stannic chloride with quinone, the same as the complex of stannic chloride with diethyl oxalate [5,8], has the empirical composition $\text{SnCl}_4 \cdot A$, and that both of these complexes exist as the dimer.

The complex of stannic chloride with 2-furaldehyde of composition $\text{SnCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$ was obtained by Pfeiffer [9]. As far as we know, the complexes of stannic bromide and titanium tetrachloride with 2-furaldehyde are not described in the literature. Complexes of stannic chloride and bromide with dioxane having a 1:2 composition were isolated by Rheinboldt and Boy [10]. The 1:1 complex of titanium tetrachloride with dioxane of composition $\text{TiCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$ has been reported [11]. On the basis of a cryoscopic study of the system $\text{TiCl}_4 - \text{C}_4\text{H}_8\text{O}_2$, one of us [12] also came to the conclusion that the complex $\text{TiCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$ exists and, in addition to this, isolated the crystalline complex $\text{TiCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$. The latter compound was also obtained later by O. Osipov and co-workers [13]. These authors measured the dipole moment of TiCl_4 in dioxane, which proved to be equal to 3.48 D.

EXPERIMENTAL

The stannic chloride and bromide, and also the titanium tetrachloride, were purified by the earlier-described method [14]. The stannic chloride had b.p. 109° (695 mm), the stannic bromide had b.p. 198° (195 mm), and m.p. 29.0° , and the titanium tetrachloride had b.p. 132.5° (699 mm). The collected fractions were distilled into ampoules [15]. The dioxane was dried over calcined CaCl_2 and then purified by repeated distillation; the

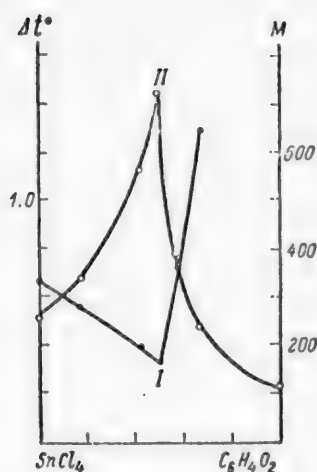


Fig. 1. Dependence of the depression (I) and molecular weight (II) on composition of the system $\text{SnCl}_4\text{-C}_6\text{H}_4\text{O}_2$ (in mole%) in p-dichlorobenzene.

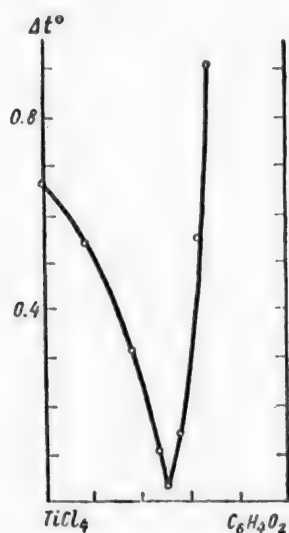


Fig. 2. Curve for the cryoscopic titration of TiCl_4 with quinone in benzene.

In forming the complex with the equimolecular composition. The curve for the dependence of the molecular weight on the composition passes through a single maximum, found at 50 mole%. The molecular weight at the singular point corresponds to a value of 725. The formula molecular weight for the monomer is 368.65, and for the dimer it is 737.30.

Consequently, both the results of a cryoscopic study of the system and the analysis data indicate that the equimolecular complex, represented by the $(\text{SnCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2)_2$, is formed in the system.

fraction boiling at 98° (693 mm) was collected, m.p. 10.8° . The 2-furaldehyde (c.p.) was distilled twice. The quinone, obtained by the oxidation of hydroquinone with a mixture of sodium dichromate and sulfuric acid, was purified by sublimation, and had m.p. 116° . The diethyl oxalate was dried over ignited copper sulfate, and then was purified by repeated distillation. The fraction boiling at 179.2° (693 mm) was collected. The benzene was purified in conventional manner and then was fractionally frozen, m.p. -5.5° . The p-dichlorobenzene was purified by repeated distillation, m.p. 53.0° .

1. System stannic chloride-quinone. In the same manner as K. Meyer [6], we isolated the complex of stannic chloride with quinone from benzene solutions. When SnCl_4 was mixed with quinone in benzene solution, the solution turned red, and after some time handsome red crystals deposited from it. The crystals were suction-filtered from the mother liquor, using a porous glass filter, then washed well with benzene, followed by drying in a vacuum-oven over P_2O_5 . The obtained complex proved to be extremely unstable, and on drying it lost its crystalline structure, changing to a yellow-green powder. Consequently, to avoid changing the composition of the complex, we proceeded in the following manner: Mixtures of stannic chloride with quinone in benzene solution were prepared using 1 mole of SnCl_4 per mole of quinone, and per 2 moles of quinone; the obtained precipitates were separated from the mother liquor and then washed rapidly with cold benzene in a special apparatus [3]. Then the precipitate was transferred to a 100-ml volumetric flask, followed by the addition of water up to the mark. The filtrate and rinse liquor were combined in another 100-ml volumetric flask, and the volume was made up to the mark with benzene. The obtained solutions were analyzed for tin, chlorine, and quinone, and the molar ratio $\text{SnCl}_4\text{:C}_6\text{H}_4\text{O}_2$ in the filtrate and in the precipitate was calculated from the analysis data. In the case of the 1:1 mixture, the molar ratio in the filtrate was equal to 0.980, and in the precipitate it was equal to 0.985, while in the case of the 1:2 mixture the molar ratio was 0.260 in the filtrate and 0.989 in the precipitate. From this data it can be seen that excess quinone is present in the filtrate from the 1:2 mixture, while the solid phase corresponds to the complex with an equimolecular composition. In the case of the 1:1 mixture, the molar ratio $\text{SnCl}_4\text{:C}_6\text{H}_4\text{O}_2$ in both the filtrate and the precipitate corresponds to the composition of the 1:1 complex. We also isolated the complex $\text{SnCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2$ from other solvents (toluene, chloroform, and carbon tetrachloride).

The results of a cryoscopic study of the system $\text{SnCl}_4\text{-C}_6\text{H}_4\text{O}_2$, made in p-dichlorobenzene, are plotted in Fig. 1. From this graph it can be seen that as quinone is added to a solution of stannic chloride in p-dichlorobenzene, up to 50 mole% the depression drops, and then it rises. At the equivalence point, the depression is equal to one-half of the original; this indicates that two molecules of stannic chloride are tied up

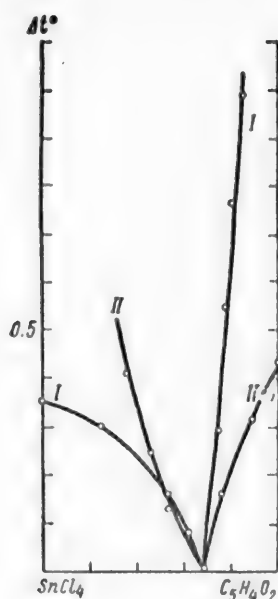


Fig. 3. Cryoscopic titration of SnCl_4 with 2-furaldehyde (I) and the reverse (II) in benzene solution.

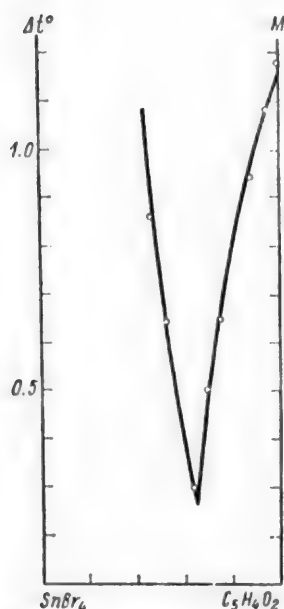


Fig. 4. Curve for the cryoscopic titration of 2-furaldehyde with stannic bromide in benzene solution.

2. System stannic bromide-quinone. We attempted to isolate the complex of stannic bromide with quinone from benzene solutions. A gradual change in the color from light- to dark-brown was observed when benzene solutions of stannic bromide and quinone (in the ratios 1:1 and 1:2) were mixed. Precipitates deposited from the solutions on standing, and changed when washed with benzene, and for this reason we were unable to analyze them.

A cryoscopic study of the system stannic bromide-quinone, made in *o*-nitrochlorobenzene (m.p. 32°), revealed that reaction, progressing with time, takes place in this system. These data also indicate that stannic bromide reacts with quinone, but they do not make it possible to judge the composition of the compound formed.

3. System titanium tetrachloride-quinone. We observed substantial heat evolution and the formation of a dark-red precipitate when a benzene solution of titanium tetrachloride was mixed with a benzene solution of quinone. This compound also proved to be unstable, the same as the compounds of the stannic halides with quinone. In establishing the composition of the complex of titanium tetrachloride with quinone, we limited ourselves to determining the molar ratio $\text{TiCl}_4:\text{C}_6\text{H}_4\text{O}_2$ in the precipitates. The results of analyzing the precipitates revealed that when equimolar amounts of TiCl_4 and quinone are mixed in either benzene or CCl_4 solution, the ratio $\text{TiCl}_4:\text{C}_6\text{H}_4\text{O}_2$ proved to be equal to 1.013, 0.916, and 0.970, and when one mole of TiCl_4 was mixed with two moles of quinone, the ratio was 0.976, 0.980, and 0.971. Consequently, these data indicate that the compound $\text{TiCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2$ is formed when TiCl_4 is mixed with quinone. On the basis of the cryoscopic measurements a diagram was obtained expressing the dependence of the depression on the composition (Fig. 2). From Fig. 2 it can be seen that as constantly increasing amounts of quinone are added to a solution of TiCl_4 in benzene the depression drops up to 50 mole%, and then it rises sharply. The depression drop is caused by a deposition of the formed compound in the precipitate. The shape of the depression curve indicates that the equimolecular compound of composition $\text{TiCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2$ is formed. The value of the depression (Δt 0.05°) at the point corresponding to the composition of this compound indicates some solubility of the compound in benzene.

4. System stannic chloride-2-furaldehyde. Finely crystalline precipitates were obtained when stannic chloride was mixed with 2-furaldehyde in benzene solution (in the ratios of 1 mole of SnCl_4 per mole of $\text{C}_5\text{H}_4\text{O}_2$ and 1 mole of SnCl_4 per 2 moles of $\text{C}_5\text{H}_4\text{O}_2$). Both chemical analysis and the cryoscopic determination of the molecular weights of the precipitates in CH_3COOH revealed that in the case of both the 1:1 and 1:2 mixtures only one complex, $\text{SnCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$, is formed, already described by Pfeiffer [9]. The results of a cryoscopic study of the system $\text{SnCl}_4-\text{C}_5\text{H}_4\text{O}_2$, conducted in benzene, are represented in the form of a depression-composition diagram (Fig. 3). From Fig. 3 it can be seen that as SnCl_4 is added to a benzene solution of 2-furaldehyde (and the reverse) the depression drops, because of the deposition of the formed compound in the precipitate, all the way up to 33 mole% SnCl_4 . The shape of the curve, expressing the dependence of the depression on the composition, and also the singular point, found at 33 mole% SnCl_4 , both testify to the formation of the compound $\text{SnCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$ (sublimes at 150°), and do not give any indications of the existence of the 1:1 compound.

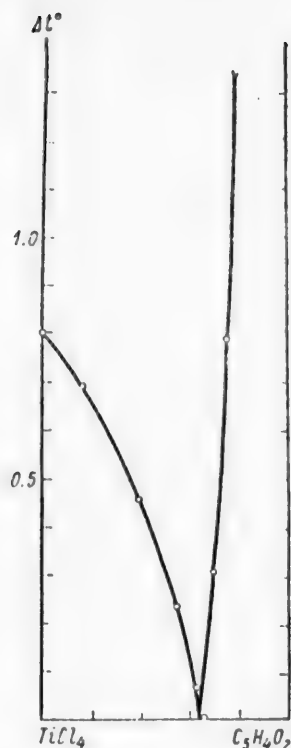


Fig. 5. Curve for the cryoscopic titration of TiCl_4 with 2-furaldehyde in benzene solution.

5. System stannic bromide-2-furaldehyde. The complex of stannic bromide with 2-furaldehyde was obtained in similar manner. The reaction between stannic bromide and 2-furaldehyde was accompanied by some evolution of heat, but less than in the case of SnCl_4 . The obtained precipitates were washed with benzene and then dried in a vacuum-oven over CaCl_2 , after which they were analyzed. The results of analyzing the precipitates obtained on mixing the components are given below.

1:2 Ratio. Found % Sn 18.56, 18.58, 18.67, 18.40; Br 51.10, 50.35, 50.95, 50.63. $\text{SnBr}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$. Calculated % Sn 18.82; Br 50.69.

1:1 Ratio. Found % Sn 18.54, 18.73, 18.75, 18.75; Br 50.33, 50.82, 50.67, 50.40. M 618, 612 (in acetic acid). $\text{SnBr}_4 \cdot \text{C}_5\text{H}_4\text{O}_2$. Calculated % Sn 22.21; Br 59.81. M 534.44. $\text{SnBr}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$. Calculated M 630.52.

Both the analysis of the precipitates and the cryoscopic determination of the molecular weights indicate that the compound $\text{SnBr}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$ is formed when stannic bromide and 2-furaldehyde are mixed in the proportions 1:1 and 1:2. The curve for the cryoscopic titration of 2-furaldehyde with stannic bromide, passing through a singular point at 33 mole% SnBr_4 , is shown in Fig. 4. The same as in the case of stannic chloride, we failed to obtain any indications of the formation of the equimolecular compound. The compound $\text{SnBr}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$ is difficultly soluble in organic solvents, deliquesces in the air, and melts (sublimes) at 117° .

6. System titanium tetrachloride-2-furaldehyde. The complex of TiCl_4 with 2-furaldehyde was also isolated from benzene solutions, where the TiCl_4 and 2-furaldehyde were taken in the proportions 1 mole of TiCl_4 per mole of 2-furaldehyde and 1 mole of TiCl_4 per 2 moles of $\text{C}_5\text{H}_4\text{O}_2$. Much evolution of heat and the deposition of yellow precipitates was observed on mixing the components. Analysis of the precipitates depositing from the 1:2 mixture gave the following results.

Found % Ti 12.49, 12.67, 12.64, 12.27; Cl 36.80, 36.63, 36.94. $\text{TiCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$. Calculated % Ti 12.54; Cl 37.13.

The analysis results obtained for the precipitates indicate that TiCl_4 reacts with 2-furaldehyde to form the compound $\text{TiCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$. Analysis of the precipitates depositing from the 1:1 mixture revealed that this precipitate also is the compound $\text{TiCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$, which suffered partial hydrolysis because of the long washing, needed to remove the excess unreacted TiCl_4 . The results of a cryoscopic study of the system TiCl_4 - $\text{C}_5\text{H}_4\text{O}_2$ are plotted in Fig. 5. The shape of the depression curve testifies to the fact that the depression drops as 2-furaldehyde is added gradually to a benzene solution of TiCl_4 , becomes equal to zero at 33 mole% TiCl_4 , and then rises sharply. The value of the depression at the equivalence point indicates that the formed compound is practically insoluble in benzene.

The complex $\text{TiCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$ sublimes at 120° without melting, is insoluble in benzene, toluene, xylene, and CCl_4 , and is soluble in acetic acid.

7. System stannic chloride-dioxane. The complexes of SnCl_4 with dioxane were obtained by adding dioxane to a benzene solution of SnCl_4 (in the molar ratios 1:1 and 1:2). Much evolution of heat and the formation of precipitates was observed when the solutions were mixed. Analysis of the precipitates gave the following results.

1:2 Mixture. Found % Sn 30.31, 28.72, 29.20, 27.60, 27.53, 27.57, 30.89, 30.35, 30.48; Cl 32.64, 32.71, 32.62, 32.77, 32.70, 34.97, 34.77, 34.69. $\text{SnCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$. Calculated % Sn 27.18; Cl 32.47.

1:1 Mixture. Found % Sn 29.90, 27.60, 27.50; Cl 30.05, 30.69, 30.61. $\text{SnCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$. Calculated % Sn 34.05; Cl 40.68.

* The Cl content was determined only in those precipitates containing approximately 27.5% tin.

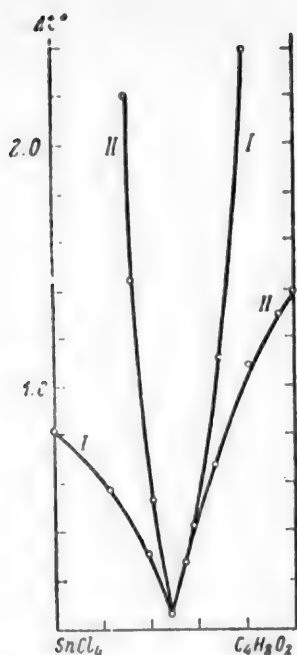


Fig. 6. Cryoscopic titration of SnCl_4 with dioxane (I) and the reverse (II) in p-dichlorobenzene solution.

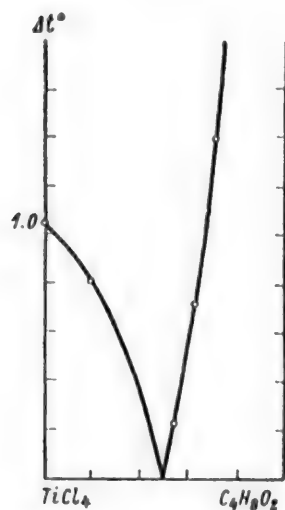


Fig. 8. Curve for the cryoscopic titration of TiCl_4 with dioxane in benzene solution.

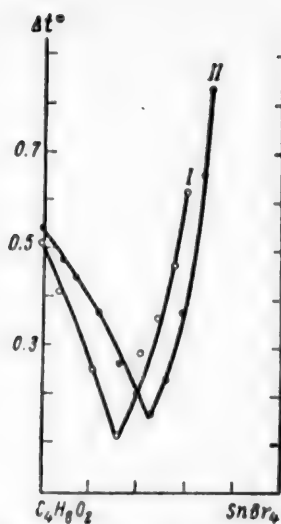


Fig. 7. Curves for the cryoscopic titration (I and II) of dioxane with stannic bromide in benzene solution.

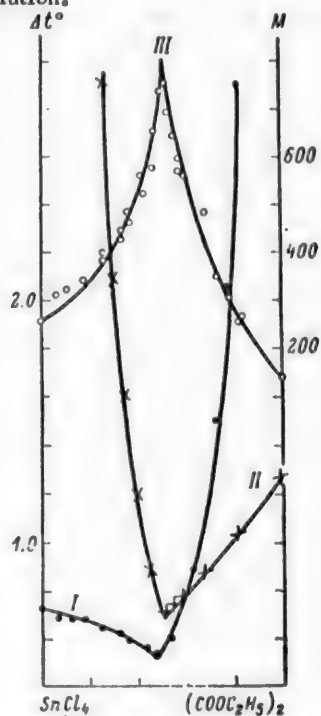


Fig. 9. Dependence of the depression (I and II) and molecular weight (III) on composition of the system $\text{SnCl}_4 - (\text{COOC}_2\text{H}_5)_2$ (in mole%) in benzene solution.

From the analysis results it can be seen that in some cases the amount of tin and chlorine in the precipitates almost agrees with that calculated for the 1:2 compound, while in other cases the amount of tin in the precipitates fluctuates between that calculated for the amount of tin in the 1:1 and 1:2 compounds. These data indicate that apparently the compounds $\text{SnCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$ and $\text{SnCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$ are formed when stannic chloride reacts with dioxane. The results of analyzing the sublimed precipitates are given below.

Found %: Sn 27.02, 26.77, 27.15; Cl 32.17, 32.50, 32.40. M 423, 428, 433 (in acetic acid). $\text{SnCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$. Calculated %: Sn 27.18; Cl 32.47. M 436.73.

Both the chemical analysis data and the molecular weight determination of the sublimate testify to the fact that the sublimate is the compound $\text{SnCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$, previously described by Rheinboldt and Boy [10].

The results of a cryoscopic study of the system $\text{SnCl}_4\text{--C}_4\text{H}_8\text{O}_2$, made in *p*-dichlorobenzene solution, are shown in Fig. 6 in the form of a depression-composition diagram. An examination of Fig. 6 reveals that as dioxane is added to a solution of stannic chloride (or the reverse) in *p*-dichlorobenzene, the depression drops up to 50 mole%, and then it rises sharply. The curves for the change in the depression are characterized by a singular point, corresponding to the equimolecular ratio of the components, i.e., to the composition of the compound $\text{SnCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$. The value of the depression (Δt 0.06°) at the equivalence point indicates that the complex $\text{SnCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$ is very slightly soluble in *p*-dichlorobenzene.

As a result, based on the analysis data and the cryoscopic measurements, we come to the conclusion that the compounds $\text{SnCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$ and $\text{SnCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$ are formed. Both compounds are white crystalline powders, practically insoluble in benzene, toluene, and xylene, and soluble in acetic acid and dioxane.

8. System stannic bromide-dioxane. The complexes of stannic bromide with dioxane were obtained by mixing benzene solutions of stannic bromide and dioxane (taken in the molecular ratios 1:1 and 1:2). Analysis of the precipitates revealed that the same compound $\text{SnBr}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$, previously obtained by Rheinboldt and Boy [10], was formed in both cases.

A crystalline product was obtained when stannic bromide and dioxane, taken in a 1:1 ratio, were mixed in the absence of a solvent.

Found %: Sn 21.71, 21.61, 21.73, 21.62; Br 59.16. $\text{SnBr}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$. Calculated %: Sn 22.54; Br 60.72.

The analysis data indicate that the obtained substance is the compound $\text{SnBr}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$.

The results of the cryoscopic study of the system $\text{SnBr}_4\text{--C}_4\text{H}_8\text{O}_2$ are shown in Fig. 7, from which it can be seen that as stannic bromide is added to a benzene solution of dioxane the depression drops in one case clear up to 33 mole% SnBr_4 (Curve I), and in the other case it drops up to 50 mole% (Curve II), after which it rises. The value of the depression at the equivalence points indicates that the 1:2 compound is less soluble in benzene than the 1:1 compound.

As a result, our data indicate that stannic bromide also reacts with dioxane to form two compounds: $\text{SnBr}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$ and $\text{SnBr}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$. These compounds are crystalline substances that show slight solubility in organic solvents.

9. System titanium tetrachloride-dioxane. The complexes of titanium tetrachloride with dioxane were obtained in the cold from benzene solutions. A pale yellow crystalline product was isolated from the 1:1 mixture, which during the process of washing and drying turned white and deliquesced. For this reason we did not analyze the product. Analysis of the precipitate isolated when the components were mixed in a 1:2 ratio gave the following results.

Found %: Ti 13.28, 13.29, 13.42; Cl 38.16, 38.24, 38.29. $\text{TiCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$. Calculated %: Ti 13.09; Cl 38.75.

The analysis data indicate that the reaction of titanium tetrachloride with dioxane yields the compound $\text{TiCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$. This compound is insoluble in benzene, xylene, toluene, and CCl_4 , and is soluble in acetic acid; it sublimes at 170°.

The results of the cryoscopic study of the system $\text{TiCl}_4\text{--C}_4\text{H}_8\text{O}_2$ are shown in Fig. 8. The curve for the dependence of the depression on the composition is characterized by a singular point, corresponding to the

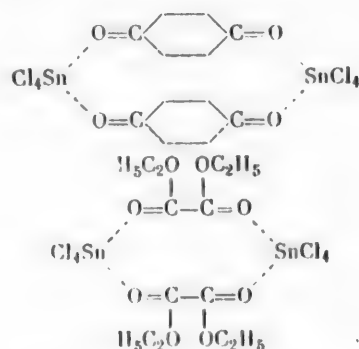
equimolecular ratio of the components, i.e., to the compound $\text{TiCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$. The absence of a depression at the equivalence point indicates that the compound $\text{TiCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$ is practically insoluble in benzene. As a result, we come to the conclusion that in the system $\text{TiCl}_4\text{--C}_4\text{H}_8\text{O}_2$, the same as in the systems $\text{SnCl}_4\text{--C}_4\text{H}_8\text{O}_2$ and $\text{SnBr}_4\text{--C}_4\text{H}_8\text{O}_2$, two compounds are formed: $\text{TiCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$ and $\text{TiCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$.

10. System stannic chloride–diethyl oxalate. The equimolecular compound of stannic chloride with diethyl oxalate was first obtained by Lewy [8]. Later, N. S. Kurnakov and N. K. Voskresenskaya [2] confirmed the composition of this compound by the fusion diagram.

We made a cryoscopic study of the system $\text{SnCl}_4\text{--}(\text{COOC}_2\text{H}_5)_2$ in benzene solution. These results are shown in Fig. 9, from which it can be seen that as stannic chloride is added to diethyl oxalate, or the reverse, the depression drops up to 50 mole%, and then it rises. This type of behavior for the depression indicates the formation of the equimolecular compound. A singular point, corresponding to the equimolecular compound, is found on the molecular weight–composition diagram. The value of the molecular weight at the singular point is approximately 805. The formula molecular weight for the monomer is 406.08, and for the dimer is 812.16. As a result, from these data it follows that the complex with a 1:1 composition is the dimer $[\text{SnCl}_4(\text{COOC}_2\text{H}_5)_2]_2$.

DISCUSSION OF RESULTS

We studied the reaction of the halides of tetravalent tin and titanium with quinone, 2-furaldehyde, dioxane, and diethyl oxalate. Here we established that SnCl_4 and TiCl_4 with quinone, dioxane, and diethyl oxalate, and also SnBr_4 with dioxane, form complexes having an equimolecular composition. The cryoscopic measurements revealed that the complexes of stannic chloride with quinone and diethyl oxalate are dimers. The structure of the dimers can be depicted in the following manner:



i.e., each quinone or diethyl oxalate molecule, manifesting a coordination capacity equal to 2, is linked to two SnCl_4 molecules.

In contrast to K. Meyer [6], we failed to obtain any indications of the existence of the compound $\text{SnCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2 \cdot \text{C}_6\text{H}_6$, containing a molecule of crystallization benzene. Apparently, K. Meyer erroneously assigned the composition $\text{SnCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2 \cdot \text{C}_6\text{H}_6$ to the complex of stannic chloride with quinone. This error was probably incurred by K. Meyer for the reason that he, the same as we, was unable to avoid decomposition of the complex during the process of removing the benzene from it. Therefore, K. Meyer, apparently desiring to retain the crystals unchanged, failed to remove all of the benzene from the complex.

We assume that the 1:1 compounds of TiCl_4 with quinone and of SnCl_4 , SnBr_4 , and TiCl_4 with dioxane, the molecular weights of which we were unable to determine, are also dimers and have an analogous structure.

2-Furaldehyde does not exhibit a coordination capacity of 2 toward the halides of tin and titanium. Compounds of composition $\text{MeX}_4 \cdot 2\text{A}$ are formed when 2-furaldehyde is reacted with SnCl_4 , SnBr_4 , and TiCl_4 . In this case, the absence of compounds with a 1:1 composition is probably due to steric hindrance, since in 2-furaldehyde the oxygen atoms are located quite close to each other.

SUMMARY

1. A study was made of the reaction of SnCl_4 , SnBr_4 , and TiCl_4 with quinone, 2-furaldehyde, dioxane, and diethyl oxalate. The following complexes were obtained: $(\text{SnCl}_4 \cdot \text{C}_6\text{H}_4\text{O}_2)_2$, $\text{SnCl}_4(\text{COOC}_2\text{H}_5)_2$, $\text{SnBr}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$, $\text{TiCl}_4 \cdot 2\text{C}_5\text{H}_4\text{O}_2$, $\text{SnCl}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$, $\text{SnBr}_4 \cdot \text{C}_4\text{H}_8\text{O}_2$, and $\text{TiCl}_4 \cdot 2\text{C}_4\text{H}_8\text{O}_2$.

2. It was established that the complexes of stannic chloride with quinone and with diethyl oxalate having an equimolecular composition are dimers, i.e., they correspond to the formula $(\text{MeX}_4 \cdot \text{A})_2$.

The theory was expressed that the 1:1 complexes of SnCl_4 , SnBr_4 , and TiCl_4 with dioxane also have the dimeric structure.

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SYNTHETIC ANALGESICS

Yu. V. Svetkin and Ya. Kamenshchik

Bashkir State University

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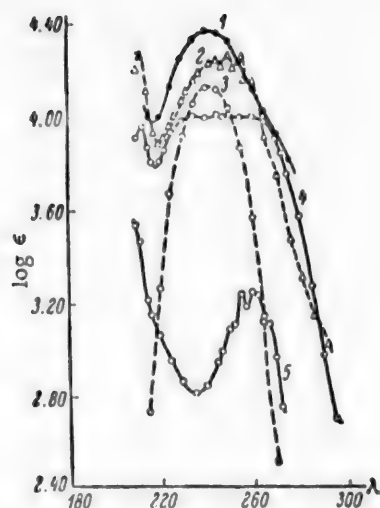
May, 1960

Original article submitted in 1959

It is known that anabesine has a high physiological activity, but its use in pharmacological practice is hindered because of its great toxicity [1]. We feel that attempts to reduce its toxicity should be directed toward reducing the mobility of the noncovalent pair of electrons on the nitrogen atom (replacement of the hydrogen on the NH group: acetylation, alkylation, acylamidation, etc.). For this reason we investigated in the present paper the condensation of anabesine with chloroacetanilide, which led to obtaining the anilide of anabesylacetic acid. The structure of this anilide was established on the basis of the chemical and spectral analysis data (see scheme on following page).

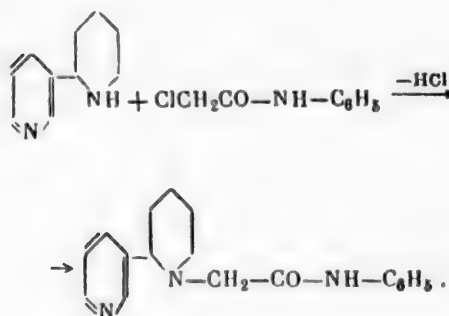
EXPERIMENTAL

Condensation of anabesine with chloroacetanilide in anhydrous alcohol. Anabesine was obtained by the method given in [2] (b.p. 107-110° at 4 mm; n_D^{20} 1.5430, d_4^{20} 1.0455). Chloroacetanilide was prepared by a method that had been worked out by one of us [3] (m.p. 134°).



Electronic absorption spectra (in the ultraviolet region) in alcohol: 1) total curve (anabasine + acetanilide); 2) curve of the condensation product; 3) curve of acetanilide; 4) curve of anabasine; 5) curve of chloroacetanilide.

Amt. of anabasine (in g)	Amt. of chloroacetanilide (in g)	Solvent (in ml)	Yield based on chloroacetanilide (in %)
10.4	8	Acetone, 50	35
10.4	10	Conc. ammonia, 50	57
4.2	6	Pyridine, 40	19
7.2	4.6	Absolute ether, 40	55
18.7	14	Petroleum ether, 40	55



A charge of 10 g of chloroacetanilide, 8 ml of anabasine, and 45 ml of anhydrous alcohol was placed in a round-bottomed flask, fitted with a reflux condenser and mechanical stirrer. The mixture was heated on the water bath for 5 hr. The alcohol was removed by distillation under reduced pressure. The residue was dissolved in 30 to 40 ml of ice-cold water, and then it was treated with cold 20% NaOH solution until alkaline. The addition of the alkali caused the formation of two layers, which were transferred to a separatory funnel. The organic layer was extracted 5-6 times with 40-ml portions of ether. The ether extracts were combined and then washed 3 times with water to remove unreacted anabasine, and then dried over fused sodium sulfate. Orange crystals deposited after about three-quarters of the ether had been distilled off, which were separated and recrystallized from a mixture of water and alcohol, m.p. 152-153° (51% yield). The compound was obtained as yellow needles, readily soluble in methanol, ethanol, and benzene, and insoluble in water, chloroform, and dioxane.

Found %: C 72.51; H 7.129; N 13.88. M 289.59. $C_{16}H_{21}ON_3$. Calculated %: C 72.28; H 7.131; N 14.21. M 295.18.

When the obtained anilide of anabasylacetic acid was hydrolyzed with concentrated HCl for 5 hr, the presence of anabasine was shown by the formation of the complex with cobalt thiocyanate. To establish fully the structure of the obtained compound, we took the electronic absorption spectra (in the ultraviolet region) of the starting substances (chloroacetanilide, acetanilide, anabasine), and of the condensation product (see figure). Employing the principle of additivity, we constructed the total curve of anabasine + acetanilide. Here we observe some shift of the first with respect to the second in the shortwave region, which is due to the influence of the adjacent CO group, but the character of the curve is approximately the same. This fact serves as additional proof that the structure of the condensation product apparently corresponds to the anilide of anabasylacetic acid.

The condensation of anabasine with chloroacetanilide in other solvents was run in a similar manner. The results of these experiments are summarized in the table.

SUMMARY

The anilide of anabasylacetic acid was obtained and characterized.

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RESEARCH IN THE FIELD OF TERPENYL PHENOLS

III. A STUDY OF THE CONDENSATION PRODUCTS OF CAMPHENE WITH PHENOL**

L. A. Kheifits, G. I. Moldovanskaya, É. V. Broun, and V. N. Belov

All-Union Scientific Research Institute of Synthetic and Natural Perfume Substances

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In recent years, terpenyl phenols have found practical application as antioxidants in synthetic and natural rubber [1-4], and for the preparation of varnishes and lacquers [5-7], emulsifiers and wetting agents [5,8], insecticides [9], and valuable perfume substances [10-16]. Almost all terpenyl phenols obtained by condensation of phenols with terpenes or by rearrangement of aryl terpenyl ethers have the form of extremely viscous gummy substances, and probably represent a mixture of various isomers.

In connection with the above, it was of interest to study in more detail the composition and structure of the products formed upon condensation of camphene with phenol in the presence of a solution of boron trifluoride in glacial acetic acid.

We discovered that the "tail" fraction (from vacuum distillation of the gummy condensation product) upon standing shows a gradual crystallization of a substance which, after separation from the oil and several recrystallizations from hexane, was isolated in the form of colorless lustrous needles with m.p. 103°.*** In some cases, crystallization is already started in the distillation process; however, prolonged storage is necessary for a fairly complete separation of this compound.

Judging by the results of elemental and functional analysis, the precipitated material is a monoalkylated product and, as we have shown, is p-isobornylphenol.****

The oil remaining after separation of the p-isobornylphenol again starts to crystallize gradually and, after many months of storage, another crystalline material, m.p. 79°, was isolated successfully in large quantities; this material in a mixed sample with the para-isomer gives a definite depression of melting point, as does a mixed sample of the corresponding 3,5-dinitrobenzoates. We have demonstrated that this second substance likewise is a monoalkylated product, in this case o-isobornylphenol.

However, in many experiments, after separation of a small quantity of the para-isomer the next material to precipitate was not the ortho-isomer, but eutectic mixtures of the two isomers with m.p. 53-54° and 62°, which could not be separated successfully by crystallizations from hexane and isopentane.

*Original Russian pagination. See C.B. translation.

**Communications I and II - see [13] and [14].

***This product was first isolated by two of us, together with É. A. Simanovskaya.

****The structure of the terpenyl group has not been established by us; however, judging by information in the literature [17], camphene in acid-catalyzed condensation with phenol forms not camphyl- but isobornylphenols.

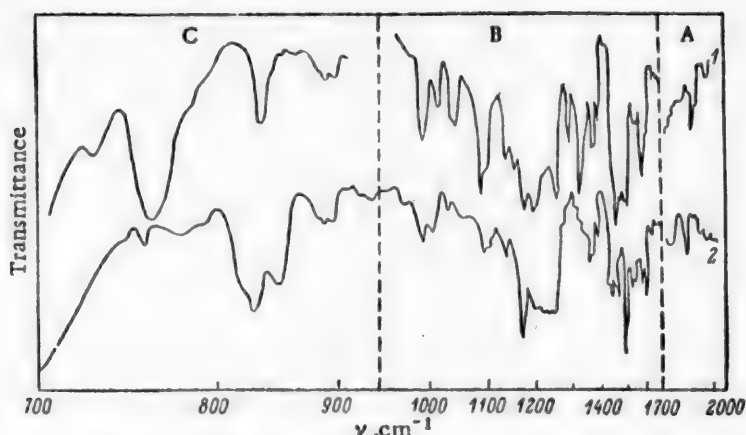


Fig. 1. Infrared absorption spectra: 1) o-isobornylphenol: A) CCl_4 solution, c 272 g/liter, d 0.484 mm; B) CCl_4 solution, c 272 g/liter, d 0.1024 mm; C) CHBr_3 solution, c 217 g/liter, d 0.1024 mm. 2) p-Isobornylphenol: A) CCl_4 solution, c 110 g/liter, d 0.484 mm; B) CCl_4 solution, c 110 g/liter, d 0.1024 mm; C) CHBr_3 solution, c 84 g/liter, d 0.273 mm.

Since the indicated method of separating the individual isobornylphenols is extremely labor and time consuming, we developed a much simpler and more convenient method of separation, based on difference of solubility of the two isomers in aqueous-alcoholic caustic. We established that in aqueous caustic (even if concentrated), both isomers are completely insoluble, but in aqueous-alcoholic caustic the p-isobornylphenol is dissolved more readily than the o-isomer. The eutectic mixture of both isomers after dissolving in petroleum ether and treatment with aqueous-alcoholic potassium hydroxide solution (containing about 20% of the KOH necessary for converting the entire mixture to phenolate) is readily separated, almost pure p-isobornylphenol being separated from the aqueous-alcoholic portion after acidification, and the o-isomer from the petroleum ether solution. Later this method was also applied successfully for the direct separation of both isomers from the gummy condensation product.

The structures of both isomers as p- and o-isobornylphenols may be inferred from their difference in solubility in aqueous-alcoholic caustic, since o-isobornylphenol, being a strongly hindered phenol, should have significantly lower solubility [18].

However, for complete assurance that the two isomers actually differ in the position of the substituents on the aromatic ring and not by a structural difference of the terpenyl group, it appeared desirable to obtain additional evidence confirming our assumption.

Since oxidation of the isomers (by the method applied by N. I. Kursanov for establishing the relative position of substituents on methylphenol [19]) in our case did not lead to clear results, we examined the isobornylphenols spectroscopically and determined the dipole moments of both isomers and of their dibromides.

We measured infrared spectra of both substances in the region of composite frequencies (1700-2000 cm^{-1}) and also in the region of nonplanar deformations of the vibrations of the C-H bonds (700-900 cm^{-1}).

The form of the spectrum in the 1700-2000 cm^{-1} region (which is characteristic for para-substituted benzenes) and also the presence of an intense band at 823 cm^{-1} [20], clearly demonstrate the para-location of the substituents in p-isobornylphenol. The skeletal vibration band of the benzene ring (1514 cm^{-1}) in the spectrum of this isomer is extremely intense and is displaced in the direction of higher frequency, which also is characteristic for para-substituted benzenes.

The form of the infrared spectrum of o-isobornylphenol in the 1700-2000 cm^{-1} region is typical for ortho-substituted benzenes. The band at 1502 cm^{-1} is less intense than for the para-isomer and has the normal frequency; in the 700-900 cm^{-1} region there is an intense band at 751 cm^{-1} , which is characteristic for

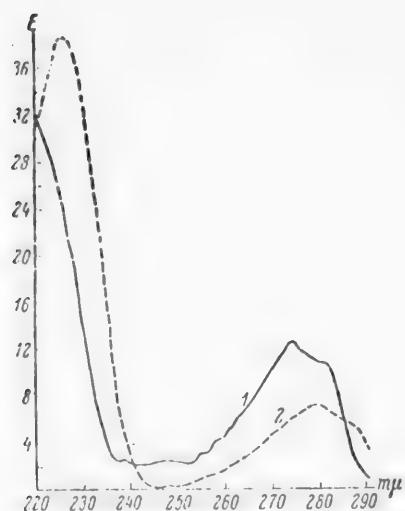


Fig. 2. Ultraviolet absorption spectra: 1) o-isobornylphenol; 2) p-isobornylphenol.

ortho-substituted benzenes [20]. It should be noted that in the o-isobornylphenol spectrum there is a band of moderate intensity at 827 cm^{-1} , which is also observed in the spectrum of o-cyclohexylphenol [21].

The characteristic splitting of the bands of the CH_3 groups in the $1340\text{--}1400\text{ cm}^{-1}$ region is indicative of the presence in both isomers of gem-dimethyl groups (doublet, 1366 and 1389 cm^{-1}), and also of isolated CH_3 groups (band at 1374 cm^{-1}).

Having preparations of p- and o-isobornylphenol, we were able to determine the quantity of these isomers in the original condensation product. Quantitative analysis was carried out by the usual method, based on the intensities at the 823 and 751 cm^{-1} band peaks. Calibration curves were obtained by means of measuring the optical density at the band peaks for solutions of various concentrations in bromoform.* By this method we established that the initial condensation product contained 70% of the ortho-isomer and 20% of the para-isomer.**

It should be noted that in the alkylation of phenol by cyclohexene with HBF_4 the ratio of ortho- to para-isomers is also 3:1 [18].

The total quantity of isobornylphenols in the condensation product, equal to 90%, is also confirmed by the results of quantitative acetylation of the initial condensation product.

The assumption that the remaining 10% consists of the isobornyl ether of phenol was not confirmed, since the infrared spectrum of the condensation product did not show the band in the 700 cm^{-1} region which is characteristic of monosubstituted benzenes. The possible content of similar compounds does not exceed 1%. The carbonyl frequency (1720 cm^{-1}) was also discovered in the infrared spectrum of the gummy product; in our opinion, this is explained by the presence of isobornyl acetate, which is apparently formed by acetylation of the camphene by acetic acid in the presence of BF_3 . The content of isobornyl acetate does not exceed 3-5%, judging by the infrared spectrum and by the ester number. After saponification of the condensation product, the carbonyl frequency in the infrared spectrum disappeared completely, and the ether number became zero.

The ultraviolet spectra of p- and o-isobornylphenol also differed from each other rather strongly; however, without additional study of the ultraviolet spectra of other p- and o-alkylphenols with bulky substituents it would be premature to judge the position of the substituents in the phenol molecule from the appearance of these spectra.

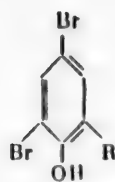
The determination of dipole moments of both isobornylphenols and their dibromides also confirms the assumption as to their structure.

The dipole moment of a p-alkylphenol should be larger than for the corresponding o-alkylphenol: thus, for p-cresol 1.57 D, for o-cresol 1.4 D. In full agreement with this, the dipole moment of p-isobornylphenol was found to be equal to 1.54 D, and the o-isobornylphenol 1.387 D.

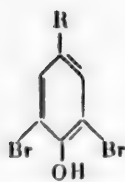
A significantly sharper difference in dipole moment should be manifested by the dibromides than by the original p- and o-isobornylphenol. With this objective, we made special preparations of the dibromides of o- and p-isobornylphenol (I and II) and measured their dipole moments: For (I) it proved to be equal to 1.47 D, and for (II) 2.40 D. The accuracy of these results was fully confirmed by measuring the dipole moments of the previously known dibromides of o- and p-cresol (III) and (IV), which we obtained from o- and p-cresol in the same way as the (I) and (II); the dipole moment of (III) proved to be equal to 1.34 D, and the dipole moment of (IV) 2.21 D.

* Absorption coefficients at the peaks of the bands analyzed: $E_{823} = 152$ liters/mole-cm, $E_{751} = 270$ liters/mole-cm; integral absorption coefficient $E = 6300$ liters/mole-cm.

** Possible error of measurement is 1-2% (of the absolute).



(I) R = isobornyl
(II) R = CH₃



(II) R = isobornyl
(IV) R = CH₃

This method of determining the location of a hydrocarbon substituent in the phenol molecule is sufficiently simple, and also can be applied successfully to other substituted phenols.

The authors consider it their pleasant duty to express deep gratitude to A. V. Iogansen for valuable advice on the spectroscopy, and to E. A. Shott-L'vova for the determination of dipole moments.

EXPERIMENTAL

Condensation of camphene with phenol. To a stirred mixture of 1 kg of phenol and 715 g of camphene at 25-30° there was added slowly 72 g of a 30% solution of BF₃ in glacial CH₃COOH; the mixture was stirred for 1 hour at 40°, 2 hours at 80°, and 3 hours at 100°. The cooled reaction mixture was washed with soda-salt solution, then with salt solution to neutral reaction; the excess phenol was distilled off, and the residue was vacuum distilled. A light yellow, gummy condensation product was obtained with content of isobornylphenols 87-88% (determined by acetylation). Yield 60-65%, b.p. 154-161° at 2 mm, d_{20}^{20} 1.0490, n_D^{20} 1.5510, ester number 10-12.

Separation of p- and o-isobornylphenol. The gummy condensation product was dissolved in petroleum ether and shaken in a separatory funnel 1 or 2 times with a 2% solution of KOH in 20% aqueous alcohol. The quantity of KOH constitutes about 20% of the quantity necessary for complete conversion of the condensation product to phenolate, and corresponds to the content of para-isomer in the condensation product. The alkaline extract was acidified with dilute H₂SO₄; the liberated oil was dissolved in hexane and washed with water. From the hexane solution by freezing at -10 to -20°, or upon standing for several days, crystalline p-isobornylphenol separated out in the form of colorless shiny needles with m.p. 103° (from hexane).

Found %: C 83.45; 83.60; H 9.74, 9.60. Bromine number 140.5. C₁₆H₂₂O. Calculated %: C 83.41; H 9.63. Bromine number 139.

3,5-Dinitrobenzoate of p-isobornylphenol. M.p. 170° (from a mixture of methanol and chloroform, 3:1 by volume).

Found %: N 6.33, 6.40. C₂₃H₂₄O₆N₂. Calculated %: N 6.60.

The petroleum ether solution, containing the isobornylphenol which had not reacted with caustic, was washed with weak aqueous acid; by freezing the petroleum ether solution at -10 to -20°, crystalline o-isobornylphenol separated out in the form of colorless shiny needles with m.p. 77° (from hexane).

The o-isobornylphenol which separated from the gummy condensation product after many months of storage had m.p. 79° (from hexane). A mixed sample with the para-isomer melted at 61-66°.

Found %: C 83.69, 83.83; H 9.54, 9.40. Bromine number 140.1. C₁₆H₂₂O. Calculated %: C 83.41; H 9.63. Bromine number 139.

3,5-Dinitrobenzoate of o-isobornylphenol. Light yellow plates with m.p. 163° (from a mixture of methanol and chloroform, 3:1 by volume). A mixed sample with the 3,5-dinitrobenzoate of the para-isomer melted at 141-144°.

Found %: N 6.68, 6.77. C₂₃H₂₄O₆N₂. Calculated %: N 6.60.

Dibromide of p-isobornylphenol. To 2 g of p-isobornylphenol there was added 50 ml of a 2 N solution of bromine in methanol saturated with NaBr; this was allowed to stand for 1 hour in the dark, after which there was added excess 10% KI solution and then sodium thiosulfate solution until the liberated iodine had been decolorized. Upon diluting with isopentane and cooling with ice, there were precipitated fine colorless crystals of 2,6-dibromo-4-isobornylphenol with m.p. 56° (from isopentane).

Found % C 49.37; H 5.31; Br 41.33. $C_{15}H_{20}OBr_2$. Calculated % C 49.50; H 5.19; Br 41.18.

Dibromide of o-isobornylphenol. Prepared similarly to the dibromide of p-isobornylphenol. After several recrystallizations from hexane, 2,4-dibromo-6-isobornylphenol was separated in the form of colorless crystals with m.p. 75.5-76.5°.

Found % C 49.29; H 5.45; Br 41.26. $C_{15}H_{20}OBr_2$. Calculated % C 49.50; H 5.19; Br 41.18.

Dibromide of p-cresol. Prepared as described above, from 2 g of p-cresol and 100 ml of brominating mixture. Upon dilution of the reaction solution by water, 2,6-dibromo-4-methylphenol precipitated at once in the form of colorless crystals. After recrystallization from petroleum ether, shiny long needles with m.p. 48-49°. Literature data: m.p. 48-49° [22].

Dibromide of o-cresol. Prepared similarly to the dibromide of p-cresol. After recrystallization from petroleum ether, 2,4-dibromo-6-methylphenol was obtained in the form of shiny long needles with m.p. 55-56°. Literature data: m.p. 57° [23].

Measurement of infrared spectra. These were measured by a single-beam spectrometer with an NaCl prism. An electronic potentiometer EPP-09 served as the recording apparatus. A description of the apparatus and its method of operation have been given earlier [24]. Solutions in CCl_4 and $CHBr_3$ were used to measure the spectra.

Measurement of dipole moments. These were measured by the heterodyne method in benzene at 25°.

SUMMARY

1. It has been shown that the alkylation of phenol by camphene in the presence of boron trifluoride takes place at the ortho- and para-positions of the phenol molecule.
2. A method has been developed for separating the ortho- and para-isomers, making it possible to recover the isomers in pure form.
3. The position of the terpenyl substituents in the separated crystalline isomers has been proved rigorously by means of infrared spectra and also by measurement of the dipole moments of the ortho- and para-isomers and of their dibromides.
4. By means of infrared spectra it has been established that the ratio of ortho- to para-isomer in the gummy product of alkylation is equal to 3.5:1.

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ALKALOIDS OF *Thalictrum minus* L.

III. STRUCTURE OF THALMINE

S. Yu. Yunusov and Z. F. Ismailov

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR

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In previous communications from our laboratory, the isolation of five alkaloids from *Thalictrum minus* L. has been reported. Structures have been proved for two alkaloids isolated from the roots of this plant - thalimine and thalimidine. Thalimine was shown to be 3,4,7-trimethoxy-5,6-methylenedioxyaporphine, and thalimidine to be 2,3,6-trimethoxy-5-hydroxyaporphine [1].

Continuing our investigation of the alkaloids of the genus *Thalictrum*, we decided to study all nine species of this genus growing in the territory of Central Asia. Data obtained up to the present time are listed in the table for the five species of *Thalictrum* whose alkaloids we are investigating.

As seen from the data in the table, the maximum accumulation of alkaloids in the above-ground portions of *T. minus* L. is observed in the initial period of vegetative growth; the alkaloid content gradually decreases with continued growth of the plant [2].

In the present article we are reporting the results of an investigation of the structure of thalimine (I), one of the alkaloids isolated from the above-ground portions of *T. minus* L.

Thalimine is a base of nonphenolic character. It has the evolved formula $C_{17}H_{13}(NCH_3)(OCH_3)_2(OH)$.

In order to elucidate the structure of the carbon skeleton of thalimine, we subjected this alkaloid to distillation with zinc dust; phenanthrene was isolated from the distilled products [3].

By the action of either acetyl chloride or acetic anhydride on thalimine, there was obtained a single optically active nonbasic diacetyl derivative of thalimine, with the composition $C_{17}H_{12}(CH_3CONCH_3)(OCH_3)_2(OCOCH_3)$.

Oxidation of this compound by concentrated nitric acid (d 1.40) gave an acid with the composition $C_{16}H_{12}O_{10}N_2$. This acid was also formed by oxidation of the initial thalimine and of des-N-methylthalimine (II) under the same conditions. By the action of diazomethane on the acid, a dimethyl ester with the composition $C_{18}H_{16}O_{10}N_2$ was formed.

Further information on the structure of thalimine was obtained by carrying out the Hoffman degradation. Upon heating the methiodide of thalimine in alcoholic caustic, optically active des-N-methylthalimine (II) was formed. This compound (II) gave a crystalline methiodide which, upon heating in alcoholic caustic, split off

Alkaloid Content of Certain Species of *Thalictrum* L. (in % of Raw Material Weight)

Name of plant and stage of growth	Place of collection	Time of collection	Alkaloid content	
			In above-ground portion	In roots
<i>T. minus</i> L.				
Start of growth	Tashkent Oblast	4/10/55	1.10	1.05
Up to budding	" "	4/17/55	0.93	1.10
Start of budding	" "	4/26/54	0.86	0.67
Budding	" "	4/29/50	0.58	0.60
Flowering	Samarkand Oblast	6/20/49	0.38	—
Fruiting	" "	7/7/49	0.34	0.64
Up to budding	Osh Oblast	7/23/53	0.16	0.36
End of growth	Dzhambul Oblast	9/26/56	0.06	0.96
<i>T. sultanbadense</i> Stapf.				
Fruiting	Tashkent Oblast	4/20/56	0.14	0.27
<i>T. simplex</i> L.				
Budding	Osh Oblast	6/2/55	0.20	2.04
Budding	Samarkand Oblast	5/14/56	0.21	1.57
Start of fruiting	Dzhalalabad Oblast	8/30/57	0.24	1.73
<i>T. foetidum</i> L.				
Start of budding	Dzhalalabad Oblast	6/22/55	0.56	0.43
Fruiting	" "	9/4/57	0.33	0.56
<i>T. isopyroides</i> C.A.M.				
Start of growth	Kaplanbek	4/4/56	—	2.93
Fruiting	Samarkand Oblast	5/12/56	0.29	1.62

trimethylamine and formed an unsaturated nitrogen-free compound $C_{13}H_{19}O_3$ (III). The presence of an alcoholic hydroxyl group in (III) was proved by obtaining the acetyl derivative which, upon saponification, gave the original material (III). By the action of phenyl isocyanate on (III) a phenylurethane of the nitrogen-free substance was formed. Upon catalytic hydrogenation of (III), the dihydro derivative (IV) was formed, indicating the presence of one double bond in the molecule of (III). Thus, the formula of the nitrogen-free substance (III) can be evolved in the form $C_{13}H_{12}(OCH_3)_2(OH)(=)$.

The dihydro derivative (IV) was easily acetylated, forming the *o*-acetyl derivative.

Very valuable information for establishing the structure of thalmine was obtained by a study of the oxidation products both of the nitrogen-free compound (III) and of its dihydro derivative (IV). Upon oxidation of (IV) by potassium permanganate [6 g-atoms of oxygen per mole of (IV)] there were formed two acids, one with the composition $C_{16}H_{14}O_6$ (V), and another, which proved to be propionic acid. The acid (V) was also formed upon oxidation of the compounds (III), (II), and (I) by potassium permanganate (in acetone solution and in acidic or neutral media), and by chromic acid. The acid (V) gave a dimethyl ester with the composition $C_{18}H_{18}O_6$. Consequently, the formula of the acid (V) can be evolved in the form $C_{12}H_6(OCH_3)_2(COOH)_2$.

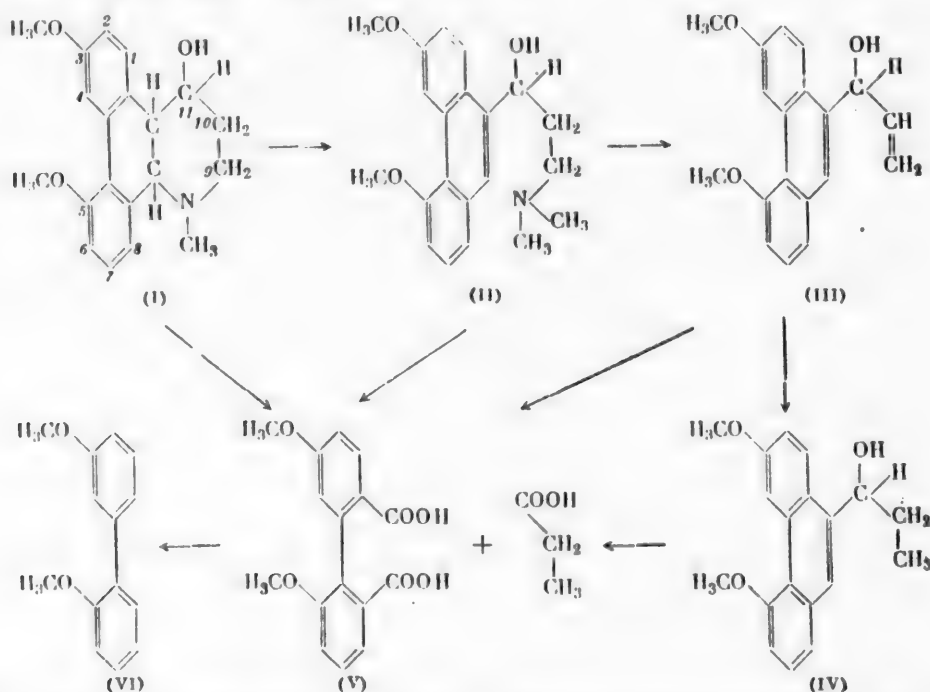
By heating the acid (V) with copper chromate catalyst in quinoline, there was obtained a neutral substance with the composition $C_{14}H_{14}O_2$ or $C_{12}H_6(OCH_3)_2$ (VI). Upon distillation of the acid with zinc dust, biphenyl was formed. Hence, the compound (VI) is a dimethoxybiphenyl, and the acid (V) is a dimethoxybiphenyldicarboxylic acid. Since the basis of the carbon skeleton of thalmine is the phenanthrene structure, it follows that upon oxidation of thalmine the acid (V) will be formed with carboxyl groups on the 2 and 2' positions of the biphenyl molecule.

For establishing the position of the methoxy groups in the acid (V), we subjected it to oxidation both by potassium permanganate and by concentrated nitric acid. In the first case, we isolated oxalic acid, and in the second case a dinitro acid. The latter proved to be a dinitrodimeoxybiphenyl-2,2'-dicarboxylic acid. Hence, in this case, simple nitration of the acid (V) occurred.

*As in original — Publisher's note.

As is evident from the above-cited oxidation experiments, both of the benzene rings in the molecule of the acid (V) behave identically toward oxidizing agents. This enables us to assume that the methoxy groups in the dimethoxybiphenyl are on the two benzene rings of the biphenyl. Such a derivative of biphenyl has 6 isomers, of which 5 are described in the literature. Since the properties of our compound do not agree with the known properties of any of the 5 isomers, the remaining possible structure is 2,3'-dimethoxybiphenyl (VI), and for the acid (V) the structure 5,6'-dimethoxybiphenyl-2,2'-dicarboxylic acid.

On the basis of the behavior we have disclosed, thalmine has the structure (I), and its breakdown may be explained in abbreviated form by the following scheme:



As is evident from the formula (I), thalmine is the first natural substance which represents a derivative of phenanthrene in combination with a derivative of piperidine. By analogy with phenanthridine, we have started with the hydrocarbon triphenylene and have named thalmine as a derivative of triphenylidine.

In this nomenclature, thalmine is 3,5-dimethoxy-N-methyl-11-hydroxyhexahydrotriphenylidine.

EXPERIMENTAL

Distillation of thalmine (I) with zinc dust. Five grams of thalmine was mixed with 50 g of zinc dust and 1 g of shredded and calcined asbestos, placed in a refractory tube, and heated to dull red heat in a stream of carbon dioxide. A brown viscous liquid was distilled off and collected in an ice-cooled receiver. At the end of the distillation the contents of the tube, and also the contents of the receiver were extracted with ether. The ether extract was washed with 2% hydrochloric acid and dried. After distilling off the ether, there remained 0.5 g of a light-brown oil distilling at 335-340°. Upon addition of alcohol, white crystals were precipitated, m.p. 95-96°. A mixed sample of this substance with phenanthrene, and also a mixed sample of the corresponding picrates did not give any melting-point depression.

Diacetylthalmine. a) One gram of thalmine was introduced into an ampoule, 2.5 ml of acetyl chloride was added, the ampoule was sealed, and the contents were mixed so that the material was dissolved. The mixture was allowed to stand for 20 days, during which it was converted to a solid mass; this was made alkaline and extracted with ether. After distilling off the ether there remained an amorphous powder, which was crystallized from a 1:2 mixture of ethanol-acetone. White needles of diacetylthalmine were obtained with m.p. 149-150° (decomp.); $[\alpha]_D - 117.5^\circ$ (c = 2.466, methanol). Yield 1.1 g.

b) One gram of thalmine was dissolved in 10 ml of freshly distilled acetic anhydride and boiled on a sand bath for 1 hr. Further treatment was carried out as indicated above. Diacetylthalmine was obtained with yield 1.25 g.

Oxidation of diacetylthalmine. Two grams of diacetylthalmine was heated in a beaker with 8 ml of nitric acid (d 1.49) on a boiling water bath until the nitric acid was completely evaporated. Then a fresh 8-ml portion of nitric acid was added and again evaporated. This operation was repeated five times. The residue was transferred to a small flask, and 5 ml of nitric acid (d 1.35) was added. Upon heating, the residue was dissolved; upon cooling, white crystals of a dinitro acid were precipitated, m.p. 248-251°. After recrystallization from acetone, m.p. 252-253°. Yield 0.8 g.

Found %: C 48.71; H 3.09; N 7.10; OCH₃ 16.40; OH 7.66. C₁₆H₁₂O₁₀N₂. Calculated %: C 48.89; H 3.08; N 7.14; 2OCH₃ 15.82; OH 7.66.

Dimethyl ester of dinitro acid. 0.5 gram of the dinitro acid was mixed with 50 ml of absolute ether; to the resulting suspension there was added 50 ml of ether containing 0.2 g of diazomethane (4 moles per mole of dinitro acid). The mixture was left for two days, until nitrogen evolution had ceased. After removal of the ether, needle-shaped crystals of the dimethyl ester were precipitated, m.p. 150-151°. Yield 0.4 g.

Found %: C 51.42; H 3.80; N 6.81; OCH₃ 26.25. C₁₈H₁₆O₁₀N₂. Calculated %: C 51.43; H 3.83; N 6.66; 4OCH₃ 26.74.

Des-N-methylthalmine (II). 1.1 grams of the methiodide of thalmine was heated with 20 ml of 30% KOH in methanol for 2 hr. The methanol was evaporated, water was added, and the des-base was extracted by chloroform. After distilling off the solvent there remained an amorphous mass with m.p. 108-112°, [α]_D -266.6° (c 2.134, methanol). Yield 0.8 g. The hydrochloride of (II) had m.p. 124-126°, and the picrate 175-177°.

Methiodide of des-N-methylthalmine. 0.5 gram of (II) was dissolved in 1 ml of methanol, and 0.5 ml of methyl iodide was added. The mixture was boiled for 6 hr. The excess methyl iodide and the methanol were distilled off. The residue was crystallized from alcohol. Fine white needles, m.p. 148-150° (decomp.). Yield 0.65 g.

Nitrogen-free compound (III). 0.5 gram of the methiodide of des-N-methylthalmine was boiled with 5 ml of 30% KOH in methanol. After 15 min, the evolution of trimethylamine began. The reaction was continued for 2 hr, after which the methanol was evaporated off and the reaction product was extracted with chloroform. The chloroform extract was washed with 5% sulfuric acid and with water. The solvent was evaporated down to a small volume (2 ml) and 2 ml of methanol was added. Upon rubbing with a rod, the nitrogen-free compound (III) crystallized, m.p. 195-198°. After two recrystallizations from 1:1 acetone-methanol mixture, m.p. 211-212°. Yield 0.2 g.

Found %: C 77.15; H 5.68; OH 5.78. C₁₂H₁₀O₃. Calculated %: C 77.55; H 6.12; OH 5.78.

Acetylation of compound (III). To 0.4 g of (III) there was added 5 ml of anhydrous pyridine and 5 ml of freshly distilled acetic anhydride. The mixture was boiled for 15 hr and then dissolved in 300 ml of chloroform. After removal of the pyridine and distilling off the chloroform, crystals were obtained with m.p. 235-237°. Yield 0.32 g.

Phenylurethane of compound (III). This was formed, upon heating (III) with phenyl isocyanate in a sealed tube at 100° for 5 hr, in the form of fine needles, m.p. 271-272°.

Hydrogenation of compound (III). One gram of (III) was dissolved in 40 ml of methanol and hydrogenated on platinum catalyst. After 3 hr, 1 mole of hydrogen had been absorbed. Warty crystals of (IV) were obtained, m.p. 172-173°. Yield 0.9 g. (IV) gave an acetyl derivative with m.p. 202-203°.

Oxidation of compound (IV). To a suspension of 1 g of (IV) in 100 ml of water there was added dropwise with constant stirring an aqueous solution of potassium permanganate [2.1 g in 150 ml of water; 6 g-atoms of oxygen per mole of (IV)] in the course of 5 hr. The mixture was allowed to stand for 20 hr, and the oxidation was completed by heating on a water bath for 5 hr. The solution was filtered off from the manganese dioxide. The precipitate was washed with 2% KOH and with water. The filtrates were combined (200 ml), washed with chloroform, and acidified with 15% sulfuric acid. The precipitated material was separated, washed with water, and

dried; m.p. 281-283° (decomp.). Yield 0.3 g. A mixed sample with the acid (V) obtained by oxidation of (I) did not give any melting-point depression. The acidic mother liquor was extracted with ether (2 liters). After distilling off the solvent, there was obtained 3 ml of a liquid, which was made alkaline with 10% KOH solution. White crystals of the potassium salt of the acid were precipitated. Yield 0.1 g. From this salt there was obtained an anilide with m.p. 104-105°. A mixed sample of this anilide with the anilide of propionic acid did not give any melting-point depression.

Oxidation of compound (III). To a solution of 1 g of (III) in acetone there was added dropwise an acetone solution of potassium permanganate (2.8 g). At the end of the oxidation the precipitated manganese dioxide was separated by vacuum filtration and washed with acetone. The precipitate was treated as indicated above. The acid (V) was isolated, m.p. 281-283° (decomp.). Yield 0.6 g.

Oxidation of thalmine (I). a) One gram of (I) was oxidized by potassium permanganate in acetone solution [8.4 g of KMnO_4 ; 26 g-atoms of oxygen per mole of (I)]. From the acetone solution there were separated warty crystals of (V) with m.p. 277-280° (decomp.). Yield 0.1 g. By treatment of the manganese dioxide precipitate there was recovered an additional 0.3 g of (V) with m.p. 277-280° (decomp.). Recrystallized from alcohol (1:50), the acid had m.p. 281-283° (decomp.).

Found %: C 63.56; H 4.65; OCH_3 20.58; OH 11.88; equiv. 154.7 $\text{C}_{16}\text{H}_{14}\text{O}_6$. Calculated %: C 63.57; H 4.66; 2OCH_3 20.53; OH 11.25; equiv. 151.1.

b) To a solution of 2 g of (I) in 10 ml of 10% sulfuric acid there was added dropwise 12.5 g of chromic anhydride in a mixture of 20 ml of concentrated sulfuric acid and 20 ml of water. The oxidation was completed by boiling on a sand bath for 4 hr. Upon cooling, the acid (V) was precipitated. Yield 0.6 g.

c) To a solution of 1 g of (I) in 100 ml of 10% sulfuric acid there was added dropwise a solution of potassium permanganate (3.8 g) in the course of 2 hr. The acid (V) was recovered with yield 0.41 g.

d) Two grams of (I) was dissolved in 20 ml of 2% hydrochloric acid, and the solution was neutralized with 2% KOH and oxidized by a solution of potassium permanganate (15.5 g in 400 ml of water). There was recovered 0.7 g of the acid (V).

Oxidation of des-N-methylthalmine (II). 1 g of (II) was dissolved in 20 ml of 5% sulfuric acid, neutralized with 2% KOH, and oxidized by potassium permanganate (8 g in 200 ml of water). There was recovered 0.4 g of the acid (V).

Dimethyl ester of acid (V). To a suspension of 1.5 g of (V) in 100 ml of ether there was added 70 ml of an ether solution of diazomethane (1.1 g). The mixture was left for a day, then washed with 2% KOH and with water, and the ether was distilled off. Upon the addition of methanol, the residue crystallized in the form of white plates with m.p. 94-95°.

Found %: C 65.48; H 5.55; OCH_3 39.11. M 329.2. $\text{C}_{18}\text{H}_{18}\text{O}_6$. Calculated %: C 65.45; H 5.45; 4OCH_3 37.57. M 330.3.

Decarboxylation of the acid (V). A mixture of 4 g of powdered copper chromate catalyst with 2 g of the acid (V) and 15 ml of freshly distilled quinoline was boiled until carbon dioxide evolution ceased, after which 300 ml of ether was added. The ether extract was filtered off from the catalyst and washed with 10% sulfuric acid, then with 2% KOH and with water. After removal of the ether there was obtained 1.2 g of crystals with m.p. 75-77° (from alcohol). After sublimation and repeated recrystallization, white fluffy needles with m.p. 79-80°.

Found %: C 78.93; H 6.43; OCH_3 26.65. M 191.8. $\text{C}_{14}\text{H}_{14}\text{O}_2$. Calculated %: C 78.47; H 6.58; 2OCH_3 28.93. M 214.2.

Distillation of the acid (V) with zinc dust. Two grams of the acid (V) was mixed with 20 g of zinc dust and 0.7 g of calcined and shredded asbestos; the mixture was placed in a refractory tube and subjected to distillation in a stream of dry hydrogen. The distilled product was dissolved in ether, filtered, washed with 2% KOH, and distilled. The partially crystallized residue (0.2 g) was sublimed at 70-80°. White platelike crystals were obtained with m.p. 65-67°. A mixed sample with biphenyl did not give any melting-point depression.

Oxidation of the acid (V). a) 0.5 gram of the acid (V) was dissolved in 50 ml of 1% KOH, and a solution of 7 g of potassium permanganate in 150 ml of water was added. The oxidation was completed by heating for 24 hr. The precipitated manganese dioxide was washed with 2% KOH and with water. The filtrates were combined and acidified with concentrated hydrochloric acid. The initial acid (V) was precipitated. Yield 0.15 g. The mother liquor was extracted with ether; after distilling off the ether from the extract, there remained a crystalline acid with m.p. 184-186°. A mixed sample of this acid and oxalic acid, or of the corresponding imides, did not give any melting-point depression.

b) One gram of the acid (V) in a beaker with 8 ml of nitric acid (d 1.40) was heated on a water bath until completely evaporated. The residue was crystallized from alcohol; m.p. 251-253°. Yield 0.8 g. A mixed sample of this acid with the dinitro acid obtained by oxidation of diacetylthamine, or a mixed sample of the corresponding dimethyl esters, did not give any melting-point depression.

SUMMARY

1. All of the five species of *Thalictrum* which we studied contained alkaloids. The alkaloid content varied markedly, depending on the place and stage of growth of the plant.
2. Distillation of thalmine with zinc dust gives phenanthrene, and oxidation of thalmine gives 5,6'-dimethoxybiphenyl-2,2'-dicarboxylic acid. The latter, upon distillation with zinc dust, gives biphenyl, and upon decarboxylation gives 2,3'-dimethoxybiphenyl (VI).
3. The Hoffman degradation of thalmine takes place in two stages with the separation of nitrogen and the formation of a nitrogen-free compound, the dihydro derivative of which is oxidized to propionic acid and 5,6'-dimethoxybiphenyl-2,2'-dicarboxylic acid.
4. The structure of thalmine has been established as a derivative of triphenylidene, namely 3,5-dimethoxy-N-methyl-11-hydroxyhexahydrotriphenylidene.

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*Original Russian pagination. See C.B. translation.

INVESTIGATION OF ACONITIC ALKALOIDS

XVII. STRUCTURE OF THE ALKALOID ZONGORINE*

A. D. Kuzovkov

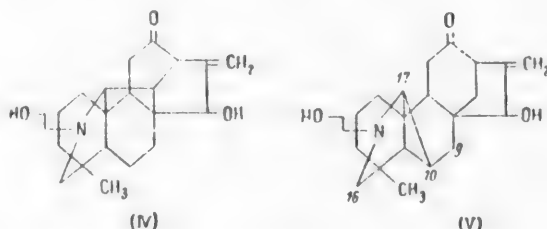
S. Ordzhonikidze All-Union Scientific Research Chemical-Pharmaceutical Institute

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Upon dehydrogenation of the alkaloid zongorine ($C_{22}H_{31}O_3N$) by selenium, we had obtained [2] a hydrocarbon of the composition $C_{18}H_{18}$ (I). Oxidation of this hydrocarbon by potassium ferricyanide led to two acids [3]: the previously known biphenyltetracarboxylic-2,3,2',4' acid (II) and a previously unknown acid (III) which, judging by analysis and the ultraviolet absorption spectrum of its trimethyl ester (IIIa), is a phenanthrenetricarboxylic acid. The simultaneous formation of (II) and (III) indicates that (III) can be only phenanthrenetricarboxylic-1,7,9 (or 10) acid. The hydrocarbon (I) was synthesized successfully [4] by the selenium dehydrogenation of 1,10-dimethyl-7-ethyloctahydrophenanthrene. These findings led us to the conclusion that the hydrocarbon (I) is 1,10-dimethyl-7-ethylphenanthrene; this makes it possible to refine formula (IV), proposed for zongorine by K. Wiesner and co-workers [5], and to replace it by formula (V) [4].



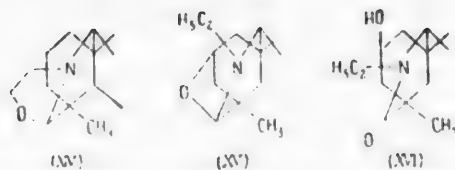
In discussing our results, K. Wiesner and co-workers [6] suggested that in the process of selenium dehydrogenation of 1,10-dimethyl-7-ethyloctahydrophenanthrene a methyl group may migrate from position 10 to position 9 (the latter being less hindered sterically), and that, consequently, the hydrocarbon (I) may be 1,9-dimethyl-7-ethylphenanthrene. This supposition led K. Wiesner to allow the possibility of the presence in the zongorine molecule of not a C_{10} - C_{17} , but a C_9 - C_{17} carbon-to-carbon bond; this compelled us to return to a study of the structure of the phenanthrenetricarboxylic acid (III). This acid shows no tendency toward the anhydride formation which would be expected with the presence of two carboxyls in the 1- and 10-positions. For comparison with the acid (III), we synthesized phenanthrenetricarboxylic-1,7,10 acid (VI) by the scheme shown on the following page.

The structure of the acids (VI), (VII), and (VIII) as represented in this scheme has been verified as follows: a) Decarboxylation of the acid (VIII) gives 1,7-dimethylphenanthrene (IX). b) The ultraviolet absorption spectra of the methyl esters of acids (III), (VI), and (VII), and of the acid (VIII) are close to each other and differ from the spectrum of the methyl ester of the biphenyltetracarboxylic acid (II). c) The acid (VII) sublimes unchanged under high vacuum, but the acid (VI) forms the anhydride (X).

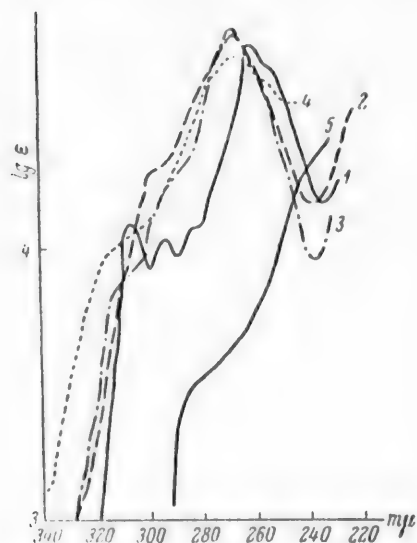
The trimethyl ester of the acid (VI) differs from the trimethyl ester of the acid (III); the acids themselves, as noted above, differ in their ability to form anhydrides. Therefore, the acid (III) is phenanthrenetricarboxylic-1,7,9 acid, and the hydrocarbon (I) is 1,9-dimethyl-7-ethylphenanthrene. These data confirm the hypothesis

*Communication XVI - see [1].





This replacement does not change the interpretation of the mechanism of oxidation of the indicated substances to lactams (XVI), and does not change the basis we gave previously for the presence in zongorine of a $>\text{CH}_2$ group in position 16 and a $>\text{CH}$ group in position 17.



Ultraviolet absorption spectra: 1) 1,7-dimethylphenanthrenecarboxylic-10 acid (VIII); 2) dimethyl ester of 1-methylphenanthrenedicarboxylic-7,10 acid (VII); 3) trimethyl ester of phenanthrenetricarboxylic-1,7,10 acid (VI); 4) trimethyl ester of phenanthrenetricarboxylic-1,7,9 acid (IIIa); 5) tetramethyl ester of biphenyltetracarboxylic 2,3,2',4' acid.

EXPERIMENTAL

Desoxyzongorine ($\text{C}_{22}\text{H}_{33}\text{O}_2\text{N}$). The substance was obtained by a Wolff-Kishner reduction, as described by Sugawara [8].

Dihydrodesoxyzongorine ($\text{C}_{22}\text{H}_{35}\text{O}_2\text{N}$). 2.8 g of desoxyzongorine was hydrogenated in methanol with Pt (from 0.1 g PtO_2). There was obtained 2.7 g of a substance with m.p. 132 to 134° (from methanol).

Found %: C 76.58; 76.61; H 10.18, 10.28. $\text{C}_{22}\text{H}_{35}\text{O}_2\text{N}$. Calculated %: C 76.50; H 10.22.

Dihydrodesoxyzongorinelactam. 2.7 g of dihydrodesoxyzongorine was oxidized in acetone solution by KMnO_4 by the method described previously [7]. The lactam was obtained with m.p. (in an evacuated capillary) 244-251° (from acetone-alcohol mixture).

Found %: C 73.22, 73.88; H 9.15, 9.14. $\text{C}_{22}\text{H}_{33}\text{O}_3\text{N}$. Calculated %: C 73.51; H 9.23.

Oxidation of dihydrodesoxyzongorinelactam. To a solution of 0.3 g of the lactam in 3 ml of glacial acetic acid there was added 0.3 g of CrO_3 in 9 ml of 90% acetic acid. After 3 hr an additional 0.2 g of CrO_3 was added. The mixture was kept overnight at 0°; then the solution was treated with potassium metabisulfite, diluted with water, and made alkaline with ammonia. The reaction product was extracted with ether. The substance melted at 167-168° (from ether). The infrared spectrum showed bands at 1636, 1712, and 1730 cm^{-1} .

Found %: C 73.93; H 8.42. $\text{C}_{22}\text{H}_{29}\text{O}_3\text{N}$. Calculated %: C 74.34; H 8.23.

α -(2-methylphenyl)- β -(2-nitro-5-methylphenyl)-acrylic acid. A solution of 10.3 g of o-tolylacetic acid (synthesized from o-xylene through xylol bromide and the nitrile) and 2.75 g of sodium hydroxide in 50 ml of methanol was evaporated under vacuum; 50 ml of benzene was added to the dry residue and then evaporated (under vacuum toward the end). To the sodium salt thus obtained there was added 25 ml of freshly distilled acetic anhydride and 11.4 g of 6-nitro-3-methylbenzaldehyde with m.p. 39-41°. For synthesis of this latter substance from m-xylene, the xylol bromide was obtained and then reacted with urotropine [hexamethylenetetramine] to form 3-methylbenzaldehyde [9], which was nitrated and separated in accordance with the directions of the patent [10]. The mixture was heated for 10 hr at 115-120°, cooled, mixed with 25 ml of water, heated gradually with stirring to 100°, and then heated at this temperature for 5 min. Upon cooling, a partially crystallized material precipitated; this was filtered off and recrystallized from glacial acetic acid. The nitro-acid was obtained in 6.2 g yield with m.p. 176-177°.

* In Beilstein's Handbuch der Organischer Chemie, Vol. 7, p. 296, this aldehyde is erroneously assigned the structure 2-nitro-3-methylbenzaldehyde. Compare F. Mayer, Ber. 47, 406 (1914).

Found %: N 4.68, 4.78. $C_{17}H_{15}O_4N$. Calculated %: N 4.71.

α -(2-Methylphenyl)- β -(2-amino-5-methylphenyl)-acrylic acid. To a solution of 6 g of the nitro-acid in 25 ml of dilute aqueous ammonia there was added a mixture obtained by adding 90 ml of concentrated aqueous ammonia to a solution of 35 g of iron sulfate in 100 ml of water. The paste obtained upon mixing was heated on a boiling bath for 30 min, then filtered. The filtrate was evaporated to half its original volume; upon neutralization of the solution with 10% sulfuric acid there was obtained 5 g of the amino acid with m.p. 193-194°.

Found %: N 5.44. $C_{17}H_{17}O_2N$. Calculated %: N 5.24.

1,7-Dimethylphenanthrenecarboxylic-10 acid. A solution of 3.55 g of the amino acid and 0.82 g of sodium nitrite in 25 ml of 5% sodium carbonate solution was added in small portions with good stirring to 200 ml of 20% sulfuric acid, cooled to 5°. The nearly transparent solution was filtered, made alkaline (pH 8-9) with sodium carbonate, and gradually heated to 100° and held at that temperature until gas evolution ceased. After acidification and extraction with ether, there was obtained 1.3 g of a substance with m.p. 189-191°. After crystallization from ether, yield 1-g, m.p. 195-196°.

Found %: C 81.59; H 5.46. $C_{17}H_{14}O_2$. Calculated %: C 81.61; H 5.64.

Sixty mg of 1,7-dimethylphenanthrenecarboxylic-10 acid, 30 mg of powdered copper [11], and 1 ml of quinoline were heated for 1.5 hr at 220-230°. After cooling, the mixture was diluted with ether and filtered. The filtrate was washed 3 times with 10% sulfuric acid, 10% sodium hydroxide, and water. After evaporation of the ether and crystallization of the residue from methanol there was obtained a substance with m.p. 82-83°. A mixture of this substance with 1,7-dimethylphenanthrene melted at the same temperature.

Oxidation of 1,7-dimethylphenanthrenecarboxylic-10 acid (VIII). a) One gram of the acid was oxidized with potassium ferricyanide under the conditions of oxidation of the hydrocarbon $C_{18}H_{18}$ [3]; the quantities of oxidizing agent and of potassium hydroxide corresponded to the quantities necessary for oxidation of 1 g of the hydrocarbon. The mixture of acids recovered after oxidation was treated with methanol. The insoluble portion was esterified by diazomethane in a mixture of methanol and ether (14 hr at 20°). The dimethyl ester of 1-methylphenanthrenedicarboxylic-7,10 acid was obtained. Yield 0.1 g, m.p. 145-146° (from methanol-chloroform mixture and then from acetone).

Found %: C 73.43; H 5.07. $C_{19}H_{16}O_4$. Calculated %: C 73.15; H 5.40.

Twenty mg of the ester was saponified by boiling for 1 hr with a 10% solution of potassium hydroxide in methanol. The solution was evaporated and the residue was dissolved in water. Upon acidification, 1-methylphenanthrenedicarboxylic-7,10 acid (VII) was obtained with m.p. 269-270°. After subliming at 230° (0.06 mm), m.p. 273.5-274°. The infrared spectrum showed bands at 1699 and 1725 cm^{-1} .

b) The mother liquors remaining after separation of the acids and formation of the methyl ester of 1-methylphenanthrenedicarboxylic-7,10 acid were combined and evaporated. The substances thus obtained were saponified by boiling for 1 hr with 25 ml of a 10% solution of potassium hydroxide in methanol. The methanol was evaporated, the residue was dissolved in 50 ml of water, and 25 ml of water was boiled off. The concentrated aqueous solution of potassium salts of phenanthrenecarboxylic acids was subjected to oxidation by potassium ferricyanide (the quantity of oxidizing agent and of potassium hydroxide corresponded to those required for oxidation of 0.5 g of the hydrocarbon). The mixture of acids recovered after oxidation was esterified by diazomethane. The reaction product, which was difficultly soluble in ether, was crystallized from methanol-chloroform mixture. The trimethyl ester of phenanthrenetricarboxylic-1,7,10 acid was obtained. Yield 0.12 g, m.p. 192-193°.

Found %: C 67.73; H 4.62. $C_{20}H_{16}O_6$. Calculated %: C 68.18; H 4.58.

Twenty mg of the ester was saponified as described in section a; the acid was sublimed at 270-290° (0.1 mm), giving the anhydride (X). The substance sublimed without melting at a temperature above 360°; the infrared spectrum showed bands at 1725 and 1767 cm^{-1} .

Sublimation of phenanthrenetricarboxylic-1,7,9 acid (III). Twenty mg of the acid obtained by saponification of the trimethyl ester was heated in vacuum at 180-200° and 0.05 mm. No change was observed. The material which had been heated showed one carbonyl band (1702 cm^{-1}) in its infrared spectrum. Sublimation was carried out at 300° (0.05 mm). The infrared spectrum of the sublimate coincided with the spectrum of material before heating.

SUMMARY

1. The trimethyl ester of phenanthrenetricarboxylic-1,7,10 acid has been synthesized.
2. The hydrocarbon $C_{18}H_{18}$ formed by dehydrogenation of zongorine is not 1,10-dimethyl-7-ethylphenanthrene, as previously supposed, but 1,9-dimethyl-7-ethylphenanthrene.
3. The presence of a secondary hydroxyl group on a six-membered ring of zongorine has been confirmed.
4. The structure of zongorine is subject to discussion.

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STUDY OF C_{15} ALKALOIDS

III. THE DECARBOXYLATION AND SYNTHESIS OF SOME ESTERS OF APHYLLINIC ACID

A. S. Sadykov and A. I. Ishibaev

Central Asian State University

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In a previous article [1], one of us reported on the synthesis of esters of matricinic acid. In the present work, results are presented on the decarboxylation of aphyllinic acid and the synthesis of some of its esters.

In investigating the crystalline product from the manufacture of anabasine sulfate in the Chirchik chemical-pharmaceutical plant, independent of the work of A. S. Labenski [2], we succeeded in isolating aphyllinic and aphyllidinic acids in the free state. The product in question is formed by treatment (in batches) of a mixture of the alkaloids of Anabasis aphylla with 40% sulfuric acid, and is accumulated in the diffusers in considerable quantities.

Having on hand more than 50 kg of the crystalline product, we proceeded to study the material more thoroughly. It was successfully established that aphyllinic and aphyllidinic acids are components of this technical product.

*Original Russian pagination. See C.B. translation.

Esters of Aphyllinic Acid

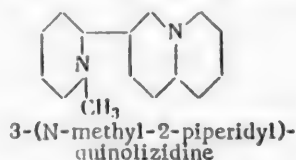
Name of ester	Starting materials			Reaction time, hr	M.p. of ester	[α] _D ²⁰	Yield, %
	aphyllinic acid, g	alcohol, ml	sulfuric acid, ml				
Methyl	2	15	0.5	3	81-82°	+ 8.9°	42
Ethyl	3	20	0.5	3.5	73-74	+11.2	35
n-Propyl	2	15	0.5	3	93-96	+28.9	25
n-Butyl	2	15	0.5	3	78-80	+17.2	27

The isolated aphyllinic acid ($C_{15}H_{26}O_2N_2 \cdot 5H_2O$) is in the form of colorless crystals. It is weakly alkaline to litmus. In the anhydrous state it is a white powder with m.p. 218-219°, [α]_D +14°, and R_f 0.33 (solvent n-butanol). The acid gives a number of well-crystallized salts: sulfate with m.p. 224-225°, dihydrochloride with m.p. 262-264°, and monomethiodide with m.p. 257-258°.

Having accumulated the two acids in considerable quantities, we first studied the reaction of decarboxylation of aphyllinic acid. From this work it was ascertained that the attempted decarboxylation of aphyllinic acid, or of its salts (bariumsalt, sulfate, and others) with or without catalysts [3,4], resulted in cyclization with the formation of aphylline in yields up to 90%.

An interesting fact should be noted: Opening the ring of aphylline (formation of aphyllinic acid) and cyclization of the latter (re-formation of the aphylline) are accompanied by a change of magnitude of the optical rotation of the base. The aphylline which we isolated from anabasine sulfate has [α]_D +27.2°; aphyllinic acid has [α]_D +14.0°; however, the aphylline obtained by cyclization of aphyllinic acid has [α]_D +16.1°. This phenomenon may be explained on the basis of what is apparently a partial isomerization of the aphylline molecule in the process of opening and closing of the lactam ring.

As already noted, aphyllinic acid and its salts are resistant to decarboxylation. We made an attempt to decarboxylate N-methylaphyllinic acid. For this purpose aphyllinic acid was methylated by formaldehyde and formic acid. N-methylaphyllinic acid was obtained in good yield. Heating this material under various conditions, either in vacuum (10 mm, 300-320° and 250-260°) or in an autoclave (in the presence of bronze) made it possible to obtain 3-(N-methyl-2-piperidyl)-quinolizidine with 10-15% yield. This substance is a stereoisomer of the alkaloid pusilline, isolated from the plant *Lupinus pusillus* [5,6].



3-(N-Methyl-2-piperidyl)-quinolizidine is a colorless thick oil; it forms a monohydrochloride with m.p. 168-170°, and also a picrate with m.p. 194-196°, [α]_D 16.2°, and R_f 0.62 (solvent n-butanol). These salts differ from those of pusilline in melting point (monohydrochloride of pusilline has m.p. 269-271°, and the picrate m.p. 183.5-185.5°).

For characterization of the aphyllinic acid we synthesized a series of its esters by interaction of the acid with the corresponding alcohols in the presence of sulfuric acid (see table). The ethyl esters of aphyllinic and aphyllidinic acids are described in the literature [7,8,9], but they were obtained by opening the lactam ring of the alkaloid.

EXPERIMENTAL

Isolation of the sulfate of aphyllinic acid. 1500 g of the technical crystalline product, a mixture of amino acid sulfates, was washed repeatedly with methanol. There was obtained 700 g of the mixture of the sulfates of aphyllinic and aphyllidinic acids. Yield 40.6%.

After three recrystallizations from hot water, the sulfate of aphyllinic acid was obtained with m.p. 224 to 225°. Yield 35%.

Aphyllinic acid. An excess of barium hydroxide was added to a solution of 400 g of the sulfate of aphyllinic acid in 1 liter of water. The resulting precipitate of barium sulfate was filtered off. The excess barium hydroxide was removed from the solution by the addition of sulfuric acid. The aqueous solution was evaporated to dryness. There was obtained 310 g of the free aphyllinic acid. Yield 92%. After three recrystallizations from hot water, the acid had m.p. 218-219° (in the anhydrous state), $[\alpha]_D +14.1^\circ$.

Dihydrochloride of aphyllinic acid. To 2 g of aphyllinic acid in 5 ml of alcohol there was added an alcoholic solution of hydrogen chloride. After recrystallization from alcohol the dihydrochloride had m.p. 262-264°.

Found %: Cl 22.20, 22.9. $C_{15}H_{26}O_2N_2 \cdot 2HCl$. Calculated %: Cl 22.35.

Monomethiodide of aphyllinic acid. To a solution of 10 g of the acid in 50 ml of methanol there was added 15 g of methyl iodide. The solution was heated for 2 hr on a water bath. Crystals of the monomethiodide precipitated after standing; after recrystallization from water it had m.p. 257-258°.

Found %: I 30.9, 32.1. $C_{16}H_{29}O_2N_2I$. Calculated %: I 31.3.

N-methylaphyllinic acid. To a mixture of 10 g of aphyllinic acid in 10 ml of water and 5 ml of 40% formaldehyde there was added gradually 4 ml of 85% formic acid. The solution was then heated on a water bath for 5 hr and evaporated to dryness under vacuum. The residue, the formate of N-methylaphyllinic acid, had m.p. 266-269°. Yield 95%. For liberation of the free acid, 10 g of the formate was mixed with 3 g of sulfuric acid, and the mixture was evaporated to dryness. The resulting product was dissolved in 50 ml of water, and an excess of barium hydroxide was added to the solution. Subsequently, the filtrate was treated with sulfuric acid for removal of barium ions. The aqueous solution was evaporated to dryness and the N-methylaphyllinic acid was recrystallized from alcohol-acetone mixture. M.p. 312-314°, $[\alpha]_D -14.6^\circ$.

Found %: N 9.90, 10.28. $C_{16}H_{28}O_2N_2$. Calculated %: N 10.00.

Decarboxylation of N-methylaphyllinic acid. Eight g of the acid was heated at 300-320° (10 mm) for 4 hr. The reaction product was dissolved in 20 ml of water and extracted with benzene. After distilling off the solvent, the remaining oil was again dissolved in benzene and was passed through a column containing aluminum oxide. Desorption from the adsorbent was carried out by successive washing, first with benzene and then with acetone. From the acetone fraction 1.2 g of 3-(N-methyl-2-piperidyl)-quinolizidine was recovered. The base was difficultly soluble in water and readily soluble in organic solvents. $[\alpha]_D -16.2^\circ$.

Found %: N 11.39, 11.31. $C_{15}H_{28}N_2$. Calculated %: N 11.44.

This compound gave a picrate with m.p. 194-196°, and also a monohydrochloride with m.p. 168-170°.

Found %: Cl 13.31, 12.5. $C_{15}H_{28}N_2 \cdot HCl$. Calculated %: Cl 13.75.

Esters of aphyllinic acid. Methyl ester. To a solution of 2 g of aphyllinic acid in 10 ml of methanol there was added 0.5 ml of sulfuric acid (d 1.84); upon cooling, hydrogen chloride was passed through the solution for 2 hr. The reaction mixture was allowed to stand until the following day. Then the alcohol was distilled off, and the remaining material was dissolved in a small quantity of water. The solution was made alkaline with potassium carbonate, and the methyl ester was extracted by ether. After drying with sodium sulfate, the ether was distilled off. The residue, 0.9 g (42%), after recrystallization from petroleum ether, had m.p. 81-82°, $[\alpha]_D +8.9^\circ$ (in alcohol).

Found %: N 9.70, 10.17. $C_{16}H_{28}O_2N_2$. Calculated %: N 10.00.

The remaining esters (ethyl, propyl, and butyl) were obtained by the same method (see table).

Ethyl ester.

Found %: N 9.47, 9.38. $C_{17}H_{30}O_2N_2$. Calculated %: N 9.52.

n-Propyl ester.

Found %: N 8.96, 9.00. $C_{18}H_{32}O_2N_2$. Calculated %: N 9.09.

n-Butyl ester.

Found %: N 8.90. $C_{19}H_{34}O_2N_2$. Calculated %: N 8.96.

SUMMARY

1. Aphyllinic acid, isolated from a technical product obtained in the production of anabasine sulfate, has been characterized. It has been established that upon attempted decarboxylation of aphyllinic acid or its derivatives, cyclization takes place with the formation of aphylline.

2. The formation of N-methylaphyllinic acid and 3-(N-methyl-2-piperidyl)-quinolizidine from aphyllinic acid has been demonstrated; the 3-(N-methyl-2-piperidyl)-quinolizidine proved to be a stereoisomer of pusilline.

3. The methyl, ethyl, n-propyl, and n-butyl esters of aphyllinic acid have been prepared and characterized.

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STUDY OF C_{15} ALKALOIDS

IV. THE STRUCTURE OF HYDROXYAPHYLLINE

A. S. Sadykov and R. N. Nuriddinov

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR

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In a previous article [1], one of us had reported on the decarboxylation of aphyllinic acid and on the preparation of certain of its esters. The present work is devoted to a proof of the structure of hydroxyaphylline, a new base isolated from the high-boiling fraction of the alkaloids of *Anabasis aphylla*.

By a careful separation of the total high-boiling alkaloids of this plant, A. P. Orekhov [2] successfully isolated (in addition to previously known alkaloids) another base with m.p. 162-164° and $[\alpha]_D^{25} +54.5^\circ$. Later, Späth and others [3], using a chromatographic method, isolated a base with m.p. 181-182° and $[\alpha]_D^{25} -32.6^\circ$. In the work of a number of authors [4-6], experimental confirmation was obtained for the correctness of the structural formulas of aphylline and aphyllidine, which were proposed by A. P. Orekhov.

*Original Russian pagination. See C.B. translation.

In separating the high-boiling fraction obtained from anabasine sulfate, we were successful in isolating (along with the already known aphylline and aphyllidine), a base with m.p. 165-167° and $[\alpha]_D^{20} +39.2^\circ$. For this base the empirical formula was determined to be $C_{15}H_{24}O_2N_2$. The base proved to be new; therefore, we named it hydroxyaphylline. Along with the hydroxyaphylline, we also isolated from the acidic solution of mixed alkaloids a nitrogen-containing substance with m.p. 182-184° and $[\alpha]_D^{20} -21.5^\circ$, having the empirical formula $C_{15}H_{20}O_2N_2$. This new compound was named oxoaphyllidine.

Hydroxyaphylline is a monobasic tertiary amine. It gives a hydrochloride with m.p. 254-255°, a perchlorate with m.p. 210-212°, and a methiodide with m.p. 223-224°. One of the nitrogen atoms in the molecule has no basic properties and is in a $>N-CO-$ group. This is confirmed by the infrared spectrum; a band is found at 1600 cm^{-1} , which is characteristic for the $>N-CO-$ group.

One of the oxygen atoms in the molecule of hydroxyaphylline is in an alcoholic hydroxyl group, as shown by the results of active-hydrogen determination (Chugaev-Tserevitinov) and by the infrared spectrum (band at 3390 cm^{-1} , which is characteristic for the hydroxyl group).

On this basis, it is possible to write an expanded formula for hydroxyaphylline:

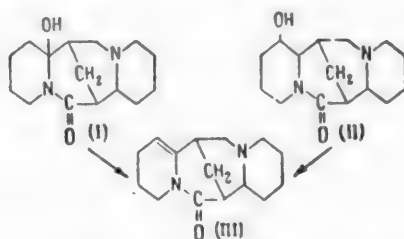


Upon heating at 170° for 3 hr, or by the action of 40% H_2SO_4 , hydroxyaphylline loses a molecule of water and is converted to aphyllidine. A similar conversion was also observed in the preparation of salts of hydroxyaphylline. This makes it possible to establish that hydroxyaphylline belongs to the lupinane group alkaloids.

The ease of dehydration of hydroxyaphylline suggested that it is simply a crystalline hydrate of aphyllidine or of a stereoisomer of aphyllidine. This hypothesis, however, was not confirmed: Aphyllidine does not give a crystalline hydrate; the conversion of hydroxyaphylline to aphyllidine takes place only by the action of 40% H_2SO_4 ; with 0.1 N H_2SO_4 the hydroxyaphylline is unchanged. This latter fact shows that the splitting of water occurs not as a result of isomerization of the hydroxyaphylline, but rather is connected with other properties of the base. Moreover, if hydroxyaphylline were a crystalline hydrate of a stereoisomer of aphyllidine, then it would necessarily have two active hydrogens. The presence of only one active hydrogen in hydroxyaphylline has been established experimentally. Hence, it has been concluded that hydroxyaphylline is not a crystalline hydrate.

The empirical formula of hydroxyaphylline corresponds to that of an N-oxide of aphylline. Assumption of the N-oxide structure would give an alternate explanation of the formation of dehydroaphylline (aphyllidine) upon dehydration. An analogous case is known in the literature [7]. As a test of our hypothesis, the N-oxide of aphylline was prepared; this proved to be entirely different from the hydroxyaphylline.

Proceeding from the considerations set forth above, we have proposed for hydroxyaphylline the most probable structural formulas, (I) and (II), which readily explain the formation of aphyllidine (III).



The choice between formulas (I) and (II) was made on the following basis. A comparison of the properties of hydroxyaphylline with those of its structural isomers hydroxylupanine [8] and lupanoline [9] (which also have hydroxyl groups) indicates a difference in the ability of these three bases to split out water. For splitting water from the two latter alkaloids it is necessary to use phosphoric or acetic anhydride, while hydroxyaphylline loses its hydroxyl very readily. In this respect it is very similar to tertiary alcohols. On this basis, we consider that the most probable structure for hydroxyaphylline is formula (I) [10].

We express sincere thanks to Yu. N. Sheinker for the determination of the infrared absorption spectrum of the hydroxyaphylline.

EXPERIMENTAL

Separation of high-boiling fraction. The high-boiling fraction was obtained by splitting anabasine sulfate with caustic and then vacuum distilling. Forty-four g of the high-boiling fraction was dissolved in 47 ml of 15% hydrochloric acid (to acidic reaction with Congo red). This acidic solution was washed repeatedly with benzene to extract nonbasic substances. Then the solution was "fractionally alkalinized," adding 1 N potassium hydroxide solution in 20-ml portions to obtain 10 fractions, which were then subjected to exhaustive extraction by benzene. After distilling off the solvent, each fraction was studied separately. The first five fractions gave crystalline bases which, after recrystallization from petroleum ether (b.p. 70-90°), had m.p. 100-103° (yield 17 g). The remaining fractions contained previously known bases (anabasine, lupinine, aphylline, and aphyllidine).

Hydroxyaphylline. For the isolation of hydroxyaphylline, 20 g of the mixture of bases with m.p. 100-103° was subjected to a secondary fractionation, separating according to basicity by the method of A.P. Orekhov [2]. Ten fractions were obtained, the first nine giving aphyllidine (m.p. 110-111°), and the tenth giving crystalline hydroxyaphylline (after distilling off the solvent and treating with acetone). Yield 0.8 g (0.36%). Hydroxyaphylline was crystallized from acetone in the form of colorless needles with m.p. 165-167°; readily soluble in benzene, alcohol, or chloroform; poorly soluble in water, acetone, or petroleum ether.

Found %: C 68.2, 68.07; H 9.09, 9.05; N 10.66, 10.56; OH 6.7, 5.52. M 262.3, 263.6. $C_{15}H_{24}O_2N_2$. Calculated %: C 68.18; H 9.09; N 10.6; OH 6.46. M 264.

Hydrochloride of aphyllidine - precipitated upon mixing an alcoholic solution of hydroxyaphylline with hydrogen chloride. After recrystallization from acetone it had m.p. 254-255°. A mixed sample with the hydrochloride of aphyllidine gave no melting-point depression.

Found %: Cl 12.48, 12.29. $C_{15}H_{22}ON_2 \cdot HCl$. Calculated %: Cl 12.56.

Perchlorate of aphyllidine - precipitated in the form of needle-shaped crystals upon mixing an acidic solution of hydroxyaphylline with a solution of sodium perchlorate. After recrystallization from water it had m.p. 210-211°. A mixed sample with the perchlorate of aphyllidine gave no melting-point depression. The base recovered after splitting the perchlorate by ammonia and recrystallization from petroleum ether had m.p. 109-111° and did not give any depression when melted with aphyllidine.

Methiodide - formed upon mixing and heating an alcoholic solution of the base and methyl iodide. After recrystallization from methanol it had m.p. 223-225°.

Action of acid on hydroxyaphylline. 0.4 g of hydroxyaphylline was dissolved in 0.1 N sulfuric acid (to acidic reaction with Congo red). The acidic solution was made alkaline and extracted with benzene. After distilling off the solvent and recrystallization from acetone, the base had m.p. 165-167°. A mixed sample with hydroxyaphylline gave no melting-point depression.

0.4 g of hydroxyaphylline was dissolved in 40% sulfuric acid (to acid reaction). The solution was made alkaline with 40% potassium hydroxide, and the precipitated crystals were removed by vacuum filtration. After recrystallization from petroleum ether, the base had m.p. 109-111°. A mixed sample with aphyllidine gave no melting-point depression.

N-Oxide of aphylline. 1.5 g of aphylline was mixed with 10 ml of 2% hydrogen peroxide and allowed to stand at room temperature. The solution was then subjected to exhaustive extraction, first by ether, then benzene, and finally chloroform (there was thus obtained 0.85 g of the original aphylline). The aqueous solution was evaporated to dryness and the residue treated with dry acetone. There was obtained a hygroscopic powder which was readily soluble in water or alcohol and insoluble in acetone, benzene, or ether. An attempt to isolate the N-oxide of aphylline in crystalline form was not successful. Therefore, the powder was dissolved in 10 ml of 10% hydrochloric acid, and 2 g of zinc dust was added with constant stirring. After filtration, extraction by ether, and distilling off the solvent, the residue was mixed with an alcoholic hydrogen chloride solution. The hydrochloride thus obtained had m.p. 207-209°, and gave no melting-point depression with the hydrochloride of aphylline.

SUMMARY

1. Two new alkaloids have been isolated from the high-boiling fraction of the total bases of *Anabasis aphylla* - hydroxyaphylline $C_{15}H_{24}O_2N_2$ and oxoaphyllidine $C_{15}H_{20}O_2N_2$.

2. Hydroxyaphylline has been established as a member of the lupinane group alkaloids, and its most probable structural formula has been proposed.

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STUDY OF C₁₅ ALKALOIDS

V. THE STRUCTURE OF OXOAPHYLLIDINE

R. N. Nuriddinov and A. S. Sadykov

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR

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In a previous article [1] we reported the isolation from the high-boiling fraction of the alkaloids of *Anabasis aphylla* of a new nitrogen-containing neutral substance, oxoaphyllidine, C₁₅H₂₀O₂N₂ (I). The results of a study of the structure of this compound are given in the present work.

Oxoaphyllidine is crystallized from ether as colorless needles with m.p. 182-184° and $[\alpha]_D -21.5^\circ$. It is readily soluble in benzene, chloroform, or alcohol, and difficultly soluble in ether. A weakly acidic solution of oxoaphyllidine decolorizes potassium permanganate solution instantly, indicating the unsaturated nature of the oxoaphyllidine. Under ordinary conditions it gives a neutral reaction and is inert toward acids or bases. Both nitrogen atoms are inactive, and are found in the form of >N-CO- groups. By passing hydrogen chloride into a methanol solution of oxoaphyllidine and then heating, there is formed a monomethyl ester of oxoaphyllidinic acid with the composition C₁₆H₂₄O₃N₂.

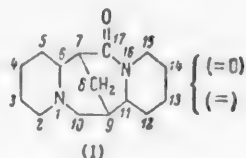
In contrast to the original compound, the monomethyl ester has basic properties and reacts as a base. This fact points out the different reactivity of the >N-CO- group. Upon hydrogenation in acetic acid solution with platonic oxide, oxoaphyllidine adds 2 atoms of hydrogen and gives a substance C₁₅H₂₂O₂N₂ with m.p. 157-159° and $[\alpha]_D -73.3^\circ$, designated as dihydrooxoaphyllidine.

Upon reduction of oxoaphyllidine in hydrochloric acid solution with platonic oxide or upon electrochemical reduction in sulfuric acid solution, 6 atoms of hydrogen are absorbed and there is formed tetrahydrodesoxy-oxoaphyllidine C₁₅H₂₄ON₂ with m.p. 83-85° and $[\alpha]_D +11.3^\circ$; picrate m.p. 182-183°.

Our experimental data are in good agreement with the literature values for oxypachycarpine (d-oxysparteine) [d-oxosparteine].

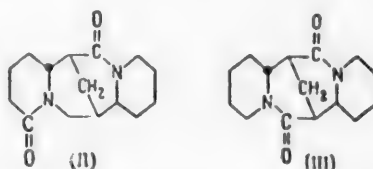
*Original Russian pagination. See C.B. translation.

A direct comparison of tetrahydrodesoxyoxoaphyllidine in the form of the base (and of its picrate) with the oxypachycarpine [d-oxosparteine] which we obtained by oxidation of pachycarpine [d-sparteine] by the method of Schopf [2] demonstrated their identity. Thus, the basic skeleton (I) has been established for oxoaphyllidine, with one of the carbonyl groups found in position 17.



It remained to establish the position of the double bond and of the second carbonyl group, which may be found in position 2 or 10. Other possibilities are excluded in view of the neutral character of oxoaphyllidine.

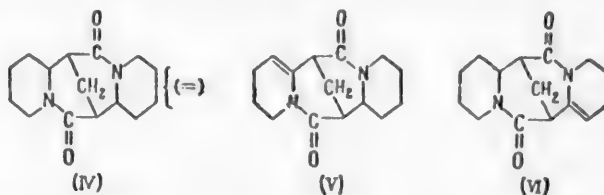
Hence, the most probable structure for the product of hydrogenation of oxoaphyllidine (dihydrooxoaphyllidine) is given by formula (II) or (III).



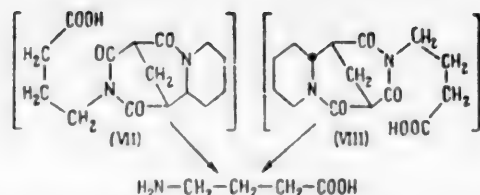
Formula (II) corresponds to an oxylupanine [oxolupanine], and (III) to an oxoaphylline (dioxysparteine) [dioxosparteine].

Of the optically active forms of oxylupanine [oxolupanine], only d-oxylupanine [d-oxolupanine] has been reported in the literature [3]. A comparison of its constants with those of dihydrooxoaphyllidine shows their difference. Therefore, formula (II) is eliminated, and for dihydrooxoaphyllidine there remains formula (III). To confirm the accuracy of the proposed formula, we oxidized aphylline by potassium permanganate in acetone solution [4] and recovered a substance with m.p. 157-159° and $[\alpha]_D -71.3^\circ$ with composition $C_{15}H_{22}O_2N_2$. This substance has not been described in the literature; we designated it as oxoaphylline, but it proved to be identical with dihydrooxoaphyllidine. This made it possible to prove conclusively that the second carbonyl group in dihydrooxoaphyllidine is located at position 10, and to propose formula (IV) for oxoaphyllidine. Simultaneously, it was established that the second carbonyl group in oxoaphylline is found in position 10.

For proof of the location of the double bond, oxoaphyllidine was oxidized by chromic acid in sulfuric acid solution with the calculated quantity of chromic acid for one double bond. This reaction resulted in the successful recovery of a substance of amphoteric character with m.p. 201-203°, giving a reaction to pyrrolidone. Heating the obtained compound to 250° resulted in splitting out water and the formation of a compound with m.p. 25°. If this latter compound is melted and allowed to stand in air, it again forms low-melting crystals with m.p. 29.5-30°. All properties of the given compound [i.e., the compound with m.p. 201-203°] are in good agreement with the literature values for γ -aminobutyric acid [5]. The identity of the recovered acid with γ -aminobutyric acid prepared by the oxidation of aphyllidine [6] was demonstrated by the determination of melting point of a mixed sample. The formation of the γ -aminobutyric acid indicates that the double bond in the molecule of oxoaphyllidine is located between the 5- and 6-carbon atoms (V) or between the 11- and 12-carbon atoms (VI).



The course of the oxidative splitting of oxoaphyllidine may be represented as follows: (V) or (VI) upon oxidation gives an intermediate amino acid (VII) or (VIII), which upon further action of the sulfuric acid is hydrolyzed and forms γ -aminobutyric acid.



Finally, the choice between formulas (V) and (VI) in favor of (V) was made on the basis of the following reasoning. By an investigation of the stereochemistry of sparteine [7-9] it was ascertained that conversion of sparteine to α -isosparteine occurs as a result of transition of the hydrogen atom on the 11-carbon atom from the trans-position to the cis-position. It was successfully established that upon hydrogenation of the double bond of dihydrosparteine, hydrogen atoms are added at the 6- and 11-carbons in the cis-position. If it is supposed that the double bond in oxoaphyllidine is found between the 11- and 12-carbons, then upon reduction the expected product would be a stereoisomer of oxypachycarpine [d-oxosparteine]; in case of complete reduction, the expected product would be a stereoisomer of sparteine, i.e., α -isosparteine. However, these substances are not obtained, which confirms the location of the double bond between the 5- and 6-carbons and the correctness of formula (V) [10].

EXPERIMENTAL

Isolation of oxoaphyllidine (I). The benzene extract which was obtained by washing the acidic solution of the total alkaloids from the high-boiling fraction of the alkaloids of *Anabasis aphylla* (see Communication IV [1]), after drying and distilling off the benzene, gave an oily product of neutral character. After repeated treatment with benzene and recrystallization from ether, crystalline oxoaphyllidine was obtained successfully in a quantity of 0.7 g.

Found %: C 69.43, 69.13; H 7.69, 7.68; N 10.68, 10.46. M 260.3, 256.4. $\text{C}_{15}\text{H}_{20}\text{O}_2\text{N}_2$. Calculated %: C 69.2; H 7.69; N 10.75. M 260.

Methyl ester of oxoaphyllidinic acid. A solution of 0.8 g of oxoaphyllidine in 30 ml of methanol was refluxed on a water bath for 8 hr while passing a stream of dry hydrogen chloride through the solution. Then the methanol was distilled off, and the residue was made alkaline with 5% sodium carbonate solution and extracted with benzene. After distilling off the solvent, the residue was dissolved in 5% sulfuric acid (to acid reaction), and the unreacted portion of the starting material was removed by benzene extraction. The acidic solution was again decomposed by 5% sodium carbonate solution and extracted with benzene. After drying and distilling off the solvent, there was obtained 0.128 g of a thick oily substance, distilling at 190° (1.1 mm).

Found %: N 9.51, 9.61. $\text{C}_{16}\text{H}_{24}\text{O}_3\text{N}_2$. Calculated %: N 9.58.

Catalytic hydrogenation of oxoaphyllidine. a) 0.4 g of platonic oxide in 20 ml of 2.5% acetic acid was agitated in a hydrogen atmosphere until saturated. Then 0.4 g of oxoaphyllidine was added to the mixture, and agitation was continued under the same conditions. A total of 36 ml of hydrogen was absorbed. At the end of the hydrogenation, the catalyst was filtered off, and the filtrate was made alkaline with 20% KOH and benzene-extracted. After distilling off the solvent, 0.38 g of dihydrooxoaphyllidine was obtained with m.p. $157-159^\circ$ (from ether), $[\alpha]_D -73.3^\circ$. The dihydrooxoaphyllidine was readily soluble in alcohol, benzene, dioxane, or chloroform, and difficultly soluble in acetone, ether, or petroleum ether.

Found %: C 67.63, 67.61; H 8.59, 8.60; N 10.55, 10.45. $\text{C}_{15}\text{H}_{22}\text{O}_2\text{N}_2$. Calculated %: C 68.7; H 8.39; N 10.68.

b) A mixture of 0.6 g of platonic oxide in 10 ml of 2 N hydrochloric acid was agitated in a hydrogen atmosphere under slight excess pressure. When hydrogen absorption had ceased, 0.4 g of oxoaphyllidine was added and agitation was continued for 10 hr under the same conditions (108 ml of hydrogen was absorbed). Further treatment of the reaction product was the same as in experiment a. After recrystallization from petroleum ether, 0.32 g of tetrahydrodesoxyoxoaphyllidine was obtained in the form of needles with m.p. $83-85^\circ$. A mixed sample with oxypachycarpine [d-oxosparteine] did not give any melting-point depression.

Picrate - precipitated upon mixing an alcoholic solution of the base and picric acid. After recrystallization from alcohol it had m.p. 180-182°. A mixed sample with the picrate of oxypachycarpine [d-oxosparteine] did not give any melting-point depression.

Found %: N 14.64; 14.44. $C_{15}H_{24}ON_2 \cdot C_6H_3O_7N_3$. Calculated %: N 14.67.

Electrochemical reduction of oxoaphyllidine. A solution of 0.5 g of oxoaphyllidine in 30 ml of 50% H_2SO_4 was subjected to reduction for 5 hr at lead electrodes (8 amp, 6 v; temperature 7-8°). The anode space was a porous clay beaker filled with 25 ml of 50% H_2SO_4 . Treatment of the reaction product was the same as in experiments a and b. There was obtained 0.43 g of crystals of tetrahydrosesoxyoxoaphyllidine, which was converted to the picrate by the usual methods. After recrystallization, the picrate had m.p. 180-182° and did not give any depression with the picrate of oxypachycarpine [d-oxosparteine].

Oxidation of aphylline. A solution of 0.53 g of aphylline in 50 ml of acetone was mixed with 5 ml of water and 5 ml of glacial acetic acid. While constantly stirring the solution, 0.9 g of powdered potassium permanganate was added. The manganese dioxide precipitate was filtered off and washed with water. The acetone was distilled off from the solution, and the residue was redissolved in 10 ml of 20% H_2SO_4 . The oxoaphylline was extracted from the solution by benzene. After distilling off the solvent and recrystallization from ether, the oxoaphylline had m.p. 157-159°, $[\alpha]_D -71.3^\circ$. Yield 0.4 g. The oxoaphylline was neutral to litmus, did not decolorize weak permanganate solution (acidic), was readily soluble in alcohol, dioxane, benzene, and chloroform, and was moderately soluble in acetone. A mixed sample with dihydrooxoaphyllidine did not give any melting-point depression.

Found %: N 10.39, 10.33. $C_{15}H_{22}O_2N_2$. Calculated %: N 10.68.

Oxidation of oxoaphyllidine. 1 g of oxoaphyllidine was dissolved in 10 ml of 50% H_2SO_4 . Over a 20-min period, 0.8 g of chromic anhydride in 20 ml of water was added to the solution; the mixture was heated first for 3 hr on a water bath, then (after the addition of 2 ml of concentrated H_2SO_4 and 6 ml of water) it was boiled for 5 hr on a sand bath. After cooling, the free and combined sulfuric acid was precipitated from the solution by adding a saturated solution of barium hydroxide; chromic hydroxide was also precipitated from the alkaline solution. After combining all of the solutions and boiling down to a small volume, the excess barium was precipitated by sulfuric acid. The filtrates, thus freed of sulfuric acid, chromic hydroxide, and barium hydroxide, were boiled to dryness. In the residue there was a thick oily substance, which was repeatedly treated with acetone. After distilling off the acetone to a small volume, crystals of γ -aminobutyric acid were precipitated (0.18 g); these were separated by vacuum filtration, washed, and recrystallized from methanol, giving m.p. 200-202°. The acid was readily soluble in acids, bases, or water, poorly soluble in alcohol, and insoluble in ether or benzene. Upon heating to 250° the γ -aminobutyric acid was converted to pyrrolidone with m.p. 25-26°, which in air gave a crystalline hydrate with m.p. 29.5-30°. A mixed sample of this γ -aminobutyric acid with that obtained by aphyllidine oxidation did not give any melting-point depression.

SUMMARY

1. Oxoaphyllidine, upon hydrogenation with platonic oxide in acetic acid solution, forms dihydrooxoaphyllidine.
2. Upon reduction of oxoaphyllidine with platonic oxide in hydrochloric acid solution, and also by electrochemical reduction, oxypachycarpine [d-oxosparteine] is formed.
3. Permanganate oxidation of aphylline gives a new compound - oxoaphylline - which is identical with dihydrooxoaphyllidine.
4. Oxidation of oxoaphyllidine by chromic acid leads to the formation of γ -aminobutyric acid.
5. The most probable structural formula for oxoaphyllidine has been proposed.

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STUDY OF C₁₅ ALKALOIDS

VI. CLEAVAGE OF APHYLLINE AND APHYLLIDINE BY SODIUM AMIDE

A. S. Sadykov and R. N. Nuriddinov

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR

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The present article is devoted to an investigation of a new type of reaction for cleavage of the >N-CO- group of certain alkaloids by means of amides of alkali metals.

Cases are known in the literature of the cleavage of nonenolizable ketones by the amides of alkali metals [1], and mechanisms of these reactions have been proposed. In studying the course of the same reaction in the case of enolizable ketones, it was successfully demonstrated that such ketones are not cleaved, but are subjected to enolization [1].

We studied the reaction in question with representatives of the C₁₅ alkaloids—aphylline and aphyllidine. Based on the structure of aphylline and aphyllidine [2], we assumed that enolization would be possible in their interaction with sodium amide; however, as shown by the study we conducted, these bases in the given case do not undergo enolization.

As a result of the interaction of aphylline with sodium amide upon heating in benzene solution, we isolated with quantitative yield a new crystalline base of the composition C₁₅H₂₇ON₃ with m.p. 262-264°. This base gives crystalline salts: hydrochloride with m.p. 295-297°, hydrobromide with m.p. 293-295°, hydroiodide with m.p. 278-280°, and picrate with m.p. 220-222°.

Under analogous conditions aphyllidine also gives a crystalline base C₁₅H₂₅ON₃, previously undescribed in the literature, with m.p. 239-240°, from which the following salts were obtained: hydrochloride with m.p. 246 to 248°, hydrobromide with m.p. 245-247°, hydroiodide with m.p. 241-243°, and picrate with m.p. 200-202°.

By comparing the empirical formulas of the obtained bases with the formulas of the original aphylline and aphyllidine (I), it is readily observed that such interaction has resulted in the addition of a molecule of ammonia, with the formation of the corresponding amides of aphyllinic and aphyllidinic acids. This is accompanied by the opening of the >N-CO- group.

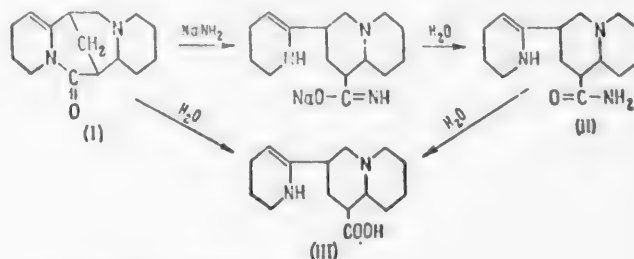
The amide of aphyllidinic acid, upon hydrogenation in acetic acid solution with platinum oxide, adds two atoms of hydrogen and is converted to the amide of aphyllinic acid.

The amides of aphyllidinic (II) and aphyllinic acids are hydrolyzed by dilute sulfuric acid, forming, respectively, aphyllidinic acid (III) and aphyllinic acid. For final confirmation of the structure of these acids,

aphyllidine and aphylline were hydrolyzed by sulfuric acid, obtaining aphyllidinic and aphyllinic acids. These acids proved to be identical to the respective acids obtained from the amides.

By a study of the reaction in question, it was successfully demonstrated that aphylline and aphyllidine are resistant to enolization which, in all probability, is caused by the rigidity of the heterocyclic ring in these bases. Similar facts for other compounds are noted in the works of L. Kh. Freidlin [3].

The course of the reaction for aphyllidine may be represented as follows:



The reaction scheme for aphylline is analogous.

EXPERIMENTAL

Cleavage of aphylline by sodium amide. To a solution of 8 g of aphylline in 30 ml of dry benzene there was added 2.5 g of pulverized sodium amide. The mixture was refluxed for 16 hr, then the reaction product was decomposed by water. The benzene layer was separated, and the water layer was chloroform-extracted. The benzene and chloroform solutions were combined, and the solvents were distilled off. The residue was treated with benzene for removal of unreacted aphylline. Then the amide of aphyllinic acid was subjected to recrystallization from alcohol-acetone mixture. M.p. 262-264°, $[\alpha]_D +19.3^\circ$. Yield 8.02 g. The amide was readily soluble in alcohol or chloroform, and poorly soluble in water, acetone, benzene, or ether.

Found %: C 67.45, 67.17; H 10.22, 9.9; N 16.08, 16.18. M 267, 263. $\text{C}_{15}\text{H}_{27}\text{ON}_3$. Calculated %: C 67.92; H 10.18; N 15.85, M 265.

Hydrochloride—precipitated upon mixing alcoholic solutions of the amide and hydrogen chloride. After recrystallization from acetone-alcohol mixture, it had m.p. 295-297°, $[\alpha]_D +15^\circ$.

Found %: Cl 20.7, 20.9. $\text{C}_{15}\text{H}_{27}\text{ON}_3 \cdot 2\text{HCl}$. Calculated %: Cl 21.0.

Hydrobromide—precipitated similarly. After recrystallization from anhydrous alcohol, it had m.p. 293 to 295°.

Hydroiodide—formed upon mixing alcoholic solutions of the amide and of hydroiodic acid. After recrystallization from acetone-alcohol mixture, it melted at 278-280°.

Picrate—precipitated upon mixing the amide with picric acid; after recrystallization from alcohol, it had m.p. 220-222°.

Found %: N 17.23. $\text{C}_{15}\text{H}_{27}\text{ON}_3 \cdot 2\text{C}_6\text{H}_3\text{O}_7\text{N}_3$. Calculated %: N 17.42.

Hydrolysis of the amide of aphyllinic acid. A solution of 4 g of the amide in 30 ml of 30% H_2SO_4 was refluxed for 8 hr. The reaction product was treated with saturated barium hydroxide solution. The precipitated BaSO_4 was filtered off, and the filtrate was washed with chloroform. After distilling off the chloroform, there remained 0.2 g of unhydrolyzed amide. The filtrate was boiled to dryness and again dissolved in water, and the excess barium was precipitated by sulfuric acid and filtered off. The mother liquor was boiled to dryness, after which the acid was purified by fractional precipitation from alcohol solution by acetone. The crystalline acid was obtained with m.p. 217-220°, readily soluble in water or alcohol, and poorly soluble in acetone, benzene, or ether.

Found %: N 9.76, 9.72. $\text{C}_{15}\text{H}_{26}\text{O}_2\text{N}_2$. Calculated %: N 10.52.

Hydrolysis of aphylline. A solution of 1.2 g of aphylline in 30 ml of 30% H_2SO_4 was refluxed for 6 hr. The

solution was then treated with barium hydroxide. The BaSO_4 precipitate was filtered off, and the filtrate was washed with ether. The excess barium was removed from the alkaline solution by acidification with sulfuric acid. After boiling the filtrate to dryness, the aphyllinic acid was purified by fractional precipitation from alcohol solution by acetone. The acid was obtained with m.p. 217-220°. A mixed sample with the aphyllinic acid obtained by hydrolysis of the amide did not give any melting-point depression.

Found %: N 9.87, 9.36. $\text{C}_{15}\text{H}_{26}\text{O}_2\text{N}_2$. Calculated %: N 10.52.

Cleavage of aphyllidine by sodium amide. A mixture of 12 g of aphyllidine in 30 ml of dry benzene and 3.8 g of pulverized sodium amide was refluxed on a water bath for 24 hr. Further treatment was the same as in the first experiment. There was obtained 11.7 g of the amide of aphyllidinic acid in the form of colorless crystals with m.p. 239-240°, $[\alpha]_D^{25} +26.5^\circ$. The amide was readily soluble in alcohol or chloroform, and poorly soluble in acetone, benzene, or water.

Found %: C 67.86, 67.80; H 9.74, 9.86; N 15.76, 15.71. M 260.8, 262.2. $\text{C}_{15}\text{H}_{25}\text{ON}_3$. Calculated %: C 68.4; H 9.5; N 15.96. M 263.

By the same methods used for obtaining salts of the amide of aphyllinic acid, the following salts of the amide of aphyllidinic acid were obtained: hydrochloride with m.p. 246-248°, hydrobromide with m.p. 245-247°, hydriodide with m.p. 241-243°, and picrate with m.p. 200-202°.

Hydrolysis of the amide of aphyllidinic acid. A solution of 10 g of the amide in 50 ml of 30% H_2SO_4 was refluxed for 6 hr. Further treatment of the reaction product was carried out as in the case of hydrolysis of the amide of aphyllinic acid. There was obtained 10 g of aphyllidinic acid with m.p. 228-230°. The acid was readily soluble in water or alcohol, and insoluble in ether, benzene, or acetone.

Found %: N 10.8. $\text{C}_{15}\text{H}_{24}\text{O}_2\text{N}_2$. Calculated %: N 10.6.

Hydrolysis of aphyllidine. A solution of 2 g of aphyllidine in 20 ml of 30% H_2SO_4 was refluxed for 4 hr. Further treatment was the same as in the hydrolysis of aphylline. Aphyllidinic acid with m.p. 228-230° was recovered. A mixed sample with the aphyllidinic acid obtained by hydrolysis of the amide did not give any melting-point depression.

Found %: N 9.83, 9.98. $\text{C}_{15}\text{H}_{24}\text{O}_2\text{N}_2$. Calculated %: N 10.6.

Hydrogenation of the amide of aphyllidinic acid. A solution of 1 g of the amide in 15 ml of 5% acetic acid was agitated with 0.2 g of platonic oxide in a hydrogen atmosphere under slight pressure. In the course of 2.5 hr, 105 ml of hydrogen was absorbed. Then the solution was filtered, made alkaline with 20% KOH, and chloroform-extracted. After distilling off the solvent, the amide of aphyllinic acid was recrystallized from alcohol-acetone mixture. M.p. 262-264°. Yield 0.8 g. A mixed sample with the amide of aphyllinic acid did not give any melting-point depression.

SUMMARY

1. A study has been made of a new type of cleavage reaction of the $>\text{N}-\text{CO}-$ group of aphyllidine and aphylline by interaction with sodium amide.
2. It has been shown that these bases are resistant to the enolization reaction. They do not form amino-compounds, but give amides of aphyllinic and aphyllidinic acids with quantitative yields.

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LETTERS TO THE EDITOR

ALKYLHALOPHENOXYACETIC ACIDS

V. G. Kryuchkova and S. V. Zavgorodnii

Voronezh State University

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Phenoxyacetic acid and its alkyl-, aryl-, and halo-substituted compounds are numbered in the hundreds; they are finding application as insecticides, herbicides, and plant-growth stimulants [1]. Of the alkylhalophenoxyacetic acids, mostly chloro- and bromo-derivatives have been described [2]. Alkylfluorophenoxyacetic acids have not been studied at all. Nevertheless, the alkylhalophenoxyacetic acids deserve the greatest attention, for some of them surpass the heteroauxins as herbicides [3,4]. Particular activity as plant-growth stimulants and herbicides is shown by fluoro-substituted phenoxyacetic acids [5,6] and by phenoxyacetic acids having a halogen in the para-position [7].

We have synthesized 12 new alkylhalophenoxyacetic acids from the corresponding alkylhalophenols and chloroacetic acid. To carry out the synthesis, 2-3 g of the monoalkylhalophenol was dissolved in 10-15 ml of 33% aqueous NaOH, 3-4.5 g of monochloroacetic acid was added, and the mixture was heated in a large test tube for 1 hr on a water bath and then cooled, diluted with water, acidified with hydrochloric acid, and treated with ether. The ether solution was extracted with 5% sodium carbonate solution, which was then acidified. The

Alkylhalophenoxyacetic Acids

Substituent in molecule of phenoxyacetic acid	Yield (%)	Melting point	Molecular weight	
			found by titration	calculated
2-Isopropyl-4-fluoro	53.8	124°	211.8, 213.0	212.1
2-sec-Butyl-4-fluoro	52.0	102-103	226.0, 225.8	226.2
2-sec-Amyl-4-fluoro	48.3	78-79	241.4, 239.6	240.2
2-Cyclohexyl-4-fluoro	54.7	120-121	250.6, 252.8	252.2
4-sec-Amyl-2-fluoro	68.3	62	241.0, 240.8	240.2
4-Cyclohexyl-2-fluoro	48.3	158-160	251.8, 252.2	252.2
2-Isopropyl-4-chloro	76.5	159	228.4, 229.2	228.6
2-sec-Amyl-4-chloro	46.1	100-101	256.8, 256.0	256.7
4-Isopropyl-2-chloro	59.7	72-73	229.0, 229.6	228.6
4-sec-Butyl-2-chloro	53.3	84-85	243.4, 241.6	242.6
4-sec-Amyl-2-chloro	46.5	59-60	255.7, 255.7	256.7
4-Cyclohexyl-2-chloro	74.5	124-125	269.4, 268.6	268.7

precipitated alkylhalophenoxyacetic acid, usually in the form of white plates or needles, was recrystallized from water, petroleum ether, or other solvent. The properties of the acids obtained are listed in the table.

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